THE METHODOLOGY OF CLINICAL SCIENCE *

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HERE IS a risk in generalising from the few facts which pprehend in our personal experience and I take this in saying that there are two main kinds of clinical ce, of which one is in danger of being overwhelmed he other Out of this distinction I shall try to create ubstance of this lecture

nical science is the planned study of disease, or of phenomena of disease, in men and women and ren who are sick It is a practical craft and this ies that the clinical scientist must possess the cular skills necessary for collecting and systematising nowledge He must possess also the opportunity to is work with such regularity and method as the sion demands. Working within the responsibility he medical care of the patient, he must do nothing h is harmful to his patient or which delays his cure s researches lead the clinical scientist to do more this, or less than this his intentions must be oved by the patient after full explanation of what store for him Approval by the patient will always nfluenced by the attitude and the opinion of the stigator and there can be no tribunal to pass judg t on what is practice and what is malpractice in the tigation of sick patients. Under these circumstances rch methods can be sanctioned *only by that faculty* h distinguishes right from wrong and which we may call conscience. This understanding of what is right what is wrong in the care of patients is part of the ssional knowledge gained in medical schools and hing hospitals from teachers, who hold their teaching for the very reason that they can transmit this ledge, with other knowledge to their assistants and nts

eturn to the two kinds of clinical science One way proach to a definition is to look at their aims The of one kind of clinical science is to know disease in a way as to enable us to infer its cause and to ct its course Seen in this way a disease is regarded equence of phenomena in a sick person arising from following on a noxious injury; and this is in accord the Aristotelian idea of the nature of things The odology of this kind of clinical science is the planned rvation of the sequence of phenomena in that er of sick people which allows us to know the non course of the disease under study from its ning to its end and to estimate and know the tions from that course. Planned observation implies use of all practicable and necessary machines of urement The knowledge it leads to has immense ical values, for to know disease in this way is the of exact therapy in professional practice. This of work might be called clinical cartography use it helps the practitioner to know where he is where he should go

e other kind of clinical science might be called al phenomenology It studies the phenomena of se or of disordered function and its aim is to explain mechanisms and their clinical significance It is rned with auricular fibrillation hunger pain, itchy or hyperpotassaemia, rather than with the diseases hich these phenomena arise. Its methodology starts identification of the phenomena and then goes on e use of experiment when possible and necessary Great benefits have come to both the science and practice of medicine by these detailed analytical studies of clinical phenomena. The knowledge gained has both increased our understanding of old diseases and pointed the way to the discovery of new diseases

Thomas Lewis did so much to establish this precise and rational study of clinical phenomena that it is tempting to use his name as an eponymous title for this kind of clinical research but Lewis's view of medicine went far beyond detailed studies of phenomena, and for that reason I have suggested that if a name has to be found it would be better to call it clinical phenomenology Thomas Lewis, however by the mere force of his personality has so influenced clinical research in this country in recent years that the study of clinical phenomena or 'states of disease' as he called them overshadows other kinds of clinical research The advantages derived from this influence have been enormous but there are grounds for believing that its dominance has led to the neglect of the planned study of disease

Clinical Observation

Before I go further I must try to make clear the different kinds of clinical observation That the instruments of clinical observation are now so disconcertingly numerous makes this all the more necessary We should keep in mind, however, that it is the essence of clinical research that while the observer should know what to look for, he should not be too absorbed to notice the unusual To grasp the significance of the unusual is an uncommon quality, and F M R Walshe stressed this idea in saying:

> It takes the exceptional mind to pass beyond the first exercises of the discriminatory tendency to pick up a hitherto unrecorded phenomenon and to grasp its significance Indeed, many a competent clinician may live out his professional existence never having made a truly original observation.

With this chastening thought in our minds we can try to separate clinical observation into its parts.

There are three main types of clinical observation, and each is as much an expression of a natural cast of mind as of a trained method of approach which is not to say that they cannot all be combined occasionally in one person's skill. How occasionally I cannot estimate for I cannot recollect having seen such a person

The first type of observation is the episodic recognition of spontaneously occurring signs of disease which we use when we diagnose and prognosticate It is the craftsman skill in seeing quickly what he knows to be significant and, as such, it grows out of experience Not all are capable of it to an excellent degree It comes best to those who talk least, and the ebullient loquacious teacher rarely possesses it. It sees the rose spot and the scabies burrow It hears the cry indicating a retropharyngeal abscess, and the wheeze of tracheal pressure. It knows when to dismiss the record of a high blood urea as a laboratory mistake or as an error in collecting the blood into a contaminated tube In its best form it works towards an economy of effort, and has its eye on what is true and what is false in new machines To this practical skill of the experienced clinical observer it is customary to give the name of clinical intuition but if this implies a kind of mystical guessing it no more deserves the name than does the skill of knowing where to find a plover's nest. It is the product not of guessing but of a sifted experience by which the significant is recognised with such rapidity that the steps of reasoning are not discernible to the uninitiated There is, of course and all too commonly, such a thing as clinical guessing, which we may suspect when we hear it bolstered up by expressions of opinion beginning with the words In my experience ' but this does not come into any of

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the categories of serious clinical observations we are discussing

This episodic or incidental type of clinical observation is not in itself a method of research It is the tool of professional practice However skilfully it may be used, it is not likely to lead either to discovery or to a decisive clarification of existing knowledge, both of which are the objects of research The truth of this will be known to those who have used the routine clinical notes of hospitals in seeking recorded facts and observations These records may have their value as a teaching instrument, but as instruments of clinical research the routine ward notes and the machinery of hospital records are almost useless

The second type of clinical observation is so rare that I may not make it evident except in examples It comes only to the mind prepared It is Coleridge's "ascertaining vision" which comes to a few "who even in the level streams have detected elements which neither the vale itself or the surrounding mountains contained or could supply" Its essence is the recognition of a new phenomenon or of a new correlation between two previously recognised phenomena Coming to those with a sufficient technical experience, it takes shape only in the minds of those endowed with imagination and insight It is near to the artist's power to see something fresh in "things we have passed a thousand times nor cared to see," but it has been an attribute also of most of the great scientists To describe it I will mention only the example of N M Gregg's brilliant recognition of the association between rubella in the pregnant woman at her eighth to tenth week of pregnancy and the congenital deformities in the child who will be born seven months later If Gregg had not systematised his observations quickly at that time, and in those circumstances, the chance might not have come again or for another hundred years or more It was fortunate that the chance came to the sensitive mind This kind of clinical observation, for which I can find no suitable name, is one of the most scintillating starting points of scientific research But we cannot order it or command it The best we can do is to recognise its possibility in the sensitive few, and to prevent its inhibition by too much teaching, its submersion by too much dogma, and its extinction by too much ritual even though it be the ritual of research

The third kind of clinical observation is what we seek to cultivate in clinical research It is clinical observation planned to answer a carefully prepared question The plan is controlled by well known criteria (*a*) that the question is worth answering, (*b*) that it has not already been answered by someone else, (*c*) that a plan of observation can be designed which is likely to provide an answer to the question, and (*d*) that the observer is the sort of man who will carry out the plan This kind of planned observation is one of the established methods of clinical research, and its scientific value is judged by the design of the plan Its purpose is to discover something, or to clarify some already existing field of knowledge In clinical medicine the latter is not less important than the former, for growth of knowledge is not inevitable, and there is, I think, such a thing as a constant growth of ignorance in medicine, which can be kept in check only by opposing to it the clarifying process of research into the validity of existing knowledge

Examples of planned clinical observation appear in various forms, but I choose the investigation of the outbreak in 1948–49 of poliomyelitis in Canadian Eskimoes at the Chesterfield Inlet because it shows how observation may on occasions rise superior to the experimental method If Peart Rhodes and their colleagues had not taken the opportunity to plan and carry out this observation the circumstances might not have occurred again, nor could anyone have designed an experiment to repeat the circumstances Its significance lay in the fact that it was an outbreak of poliomyelitis in a soil community, the like of which, with the adv the aeroplane, we are not likely to see again The p was unique It showed a case incidence of paraly 185 per 1000 of the population, 1 in 20 of the popu died, no children under the age of four years paralysed, and the epidemic reached its heig February with the mean temperature at −31°F was something unparalleled in the recorded epidem of the disease, and the success of the observ depended on the team of five medical men who flew Toronto to the scene of the epidemic and carried plans into effect There are many other examp planned clinical observation, in more obvious fie inquiry such as controlled therapeutic trials and s in prognosis, but the essential features of all a choice of question worth answering, the definitio limitation of what is to be observed, the tr and character of those who will make the observation the arrangements by which the material for obser is collected, or by which observers go to the ma to make their observations

W A Lister's planned observation of the straw naevus in 1938 will serve as a very straightfo example of design and accuracy The opening wo his simple but near perfect paper are worth noting

> "The idea of this investigation arose at a meeting dermatological section of the Royal Society of Medicine, Dr Barber showed an infant who presented a very number of prominent naevi I was struck by the uncer of all those present as to the best line of treatment adopted, and as to what would happen if nothing were (*Lancet*, 1938, i, 1429)

He thereupon designed his observation—which l five years, and comprised 77 patients—by whicl knowledge of the natural history and treatment c naevus has been established

Planned Observation of Disease

In describing planned observation of a disease th a danger that I create for it an artificial category danger is overcome if we assume that in some ci stances the researcher may use more than one tr skill He may for example be both a trained cl observer and a biochemist, or a morbid anatomist the combination rarely exists Precise clinical observ of a disease, carried out to a prearranged plan, tak much time and energy that the observer has little c of being competent in a second technical field

Planned observation of a disease is simplified i noxious agent and the time of the injury are know it is not the rôle of the clinical scientist to stud nature of the noxious agent That work now pro devolves upon the microbiologist, the chemist, physicist, and the pharmacologist Nor is it the r the clinical scientist to be morbid anatomist or e mental pathologist, who sees disease not as the c scientist sees it Their concepts of disease are ess to the progress of knowledge, and medicine could n exist nor advance without them, but it falls t clinical scientist to see disease as the sequence of ph ena in a living being which follows consequentially fr injury, and, in identifying and measuring the pheno results, to create a corpus of exact knowledge whic be applied in the practice of medicine He ma course of the disease by this sequence of pheno subjectively interpreted by the patient and objec identified by himself His main task is to plac phenomena in temporal and in quantitative relatio with each other This leads him to know the cours disease as it may be expected commonly to occur. next task is to determine the variations from that and to find correlations between these variation ætiological factors or alternative treatments ssible he uses statistics to express these variations He es statistical estimates of variations also in designing e extent of his study If the disease under study is e which varies little in its course he limits his number examples. If the course of the disease has many riations—or a wide "lunatic fringe," as the clinical ientist may call it in his despondent mood—he takes is into consideration in making his estimate of the umber of patients to be taken into his study and then oceeds towards that goal If he takes less than he needs s study is deceptively incomplete If he takes more an he needs he wastes his time In this way he plans s study of disease, and with one research finished he asses on to study another disease In this way he comes know disease as a predictable sequence of events, and he knowledge gained becomes the basis the only basis y which the underlying processes of disease in the living atient can be rationally interpreted.

I may be setting my aim too high in describing this ethod of study or this method of study may have less ientific value than I think it has; but assuming that t is a necessary and valuable instrument for one kind of linical research I believe it to be greatly neglected part from a few elementary observations on pulse and emperature, how little we know about the detailed ourse of disease. How rarely does a clinical investigator t through an illness recording the observations and nstrumental measurements for himself How seldom oes the young physician sit through a night recording he pattern of behaviour, of delirium or of sleep in a atient with encephalitis. How infrequently does the oung surgeon train himself in diagnosis by sitting at the edside of a man with ruptured duodenal ulcer to measure he fluctuation of his signs and symptoms during the eriod while the operation is prepared If the illness be rolonged how rarely do we design our observations with regularity of twelve hourly or even daily intervals Most of us come to the patient to observe only the phenomena which custom has predetermined for us, or we take the observations second hand from others who have recorded them for us I am conscious of this in confessing that I myself know very few diseases in this discriminating manner which satisfies my scientific conscience For example, I could not to my own satisfaction, describe measles, or leukaemia or acute rheumatism, or primary herpetiform stomatitis, with their hour to hour or day to-day sequence of significant phenomena precisely determined, measured and accurately recorded Yet this kind of knowledge is one of the bases on which scientific clinical medicine is built It may not reveal and unfold any new natural laws, but the practice of *rational medicine relies on it* for without the power to predict the natural course of a disease, advice and treatment will remain at the mercy of unsubstantial opinions

My claim is that clinical science should correct the bias which has been imposed upon it by dominance of the experimental study of phenomena, and that a few young clinical scientists should be trained in the exact observation and measurement of disease If it be asked what value can these have since diagnosis and treatment are the end all and be-all of practical medicine, my reply would be that it would bring mature and trained observers to the bedsides of patients and that in those circumstances new significant phenomena are likely to be discovered. Even if no new discoveries be made in this way it will at least result in a contemporary knowledge of disease and illness, for the pattern of these changing as they do in the new environments which man creates for himself are not static and eternal

The inaccuracy and inadequacy of our recorded knowledge about disease and illness will become evident if we consult a few examples in textbooks and journals Nowhere in medical literature can I find a complete coherent account of the sequence of clinical events which follows the burnings of a man, a woman, or a child If convulsions occur after burning is their frequency related to the age of the patient or to the extent of the burn? Is the time-incidence of the convulsion, if it does occur limited to the second day of the illness? There is no recorded answer to these questions. Many studies of isolated phenomena of burns have been successfully pursued, but the close relationship of one phenomenon with another has not been established That this should be the case in a disease so easy to observe and to measure is an index both of our ignorance and of faulty observation

On the other hand when we hear a young clinician say after examining and observing a suspected case of meningococcal septicæmia, 'I have been watching the appearance and measuring the changing outline of these purpuric spots over the last six hours, and from this evidence I know that this illness is not meningococcal septicæmia because this illness is at its fiftieth hour and the purpuric spots of meningococcal septicæmia are not that shape at this hour of the illness —when we hear him describing his observations in that way we know that he is heading in the direction of being a clinical scientist But there are many hindrances to this training and many obstacles to that kind of clinical work, which I must now attempt to discuss

Hindrances

This talk about scientists may build them up too much No sensible young man starts out to be a clinical scientist By accident or opportunity he later finds himself heading in that direction and follows the stream; or he comes under the personal influence of someone he likes and wishes to imitate or he is just that ort of chap who must do research because he has a passion for getting things clear in his own mind or for seeing how things tick over and finding no other outlet or way of doing it he tries his hand at clinical research He equips himself to become a clinical scientist and then he is between the physical scientists, who do not understand what he does and the practitioners of medicine and surgery who try to understand what he does He seeks a job either as a full time professional research worker or by combining research with some routine clinical practice The latter is the more difficult path to follow particularly in that clamouring kind of hospital which is lively with many conferences and other distractions. But he may order his life successfully by arranging clearly demarcated periods or days, in the way that Victor Horsley did, when he collects and systematises his *observations*

Hindrance to clinical research lies less in the claims of other clinical responsibilities than in the prevailing attitude of mind towards it—the climate of opinion, as it is now called This attitude of mind begins to take shape in medical schools, where the undergraduate thinks of medical research only as an affair of animal experiment and laboratories (I must exclude from this generalisation the three, or perhaps four *alpha* schools in this country which present a more wholesome picture of research) In the teaching hospitals he is immediately engaged in the excitements of diagnostic medicine, and his teachers are those whose skill is mainly in that branch of medicine. He runs into the danger of confusing clinical science with something called clinical investigation ' and of regarding scientific method as synonymous with the use of diagnostic machinery These misleading impressions are intensified by his preparation for final examinations with their diagnostic exercises as ' long cases ' and short cases.

These impressions about the attitude towards clinical research are strengthened by my experience on a regional hospital board committee which reviews applications for research grants from members of the medical staffs of the hospitals The applications come almost entirely from members of the clinical staffs, and they fall roughly into four categories The majority of applications are for the employment of morbid anatomists, or biochemists, or technicians to do some laboratory research which the clinicians wish to have carried out but in the techniques of which they themselves have had no training The second category consists of requests for secretarial help in *retrospective studies of hospital records* The third category is the request for diagnostic machinery The smallest category is the request for the assistance of a clinical research worker to enlarge and complete a piece of clinical research which is already under way, and which the applicant is conducting for himself

With monies now available from the universities, from endowment funds of hospitals, from the Government research councils, and from the educational trusts, the opportunities for clinical research are now beyond the dreams of what might have been considered possible thirty years ago We can therefore look forward with great interest to the directions in which these forces will flow Human nature being what it is, and human institutions what they are, we must expect that the opportunities will attract those who regard the publication of a research paper as a kind of higher diploma which will increase the chance of their being promoted to a higher clinical post Others will use the opportunities to get from these resources the extra help they need for their routine clinical work in hospitals These frailties can be easily humoured and helped in other ways than by calling them research , but if they must be called research then we must find another name for the kind of work a man does when he devotes himself to the planned and patient observation of disease, which is guided by a substantial working hypothesis

Behind all these opportunities and arrangements I see the urgent need for a due proportion of young doctors who will become physicians and surgeons and family practitioners to be trained in this kind of work otherwise we shall face the position of which E D Adrian warned us last year

> "The pathologists and biochemists will find," he said, "that their time is taken up with measurements of uncertain value in which they are not specially interested and the final result may well be that the work is turned over to specially trained technical experts who are the last people to give a dispassionate judgment on the value of what they are doing"

He went on to indicate the cure for this in saying "The point, surely, is that if such data are to be valuable there must be the right people to consider them"

We are now concerned with the selection, the training, and the working conditions of these right people This brings me back to where I started We are not likely to lack a sufficient number of the right people trained in the study of isolated clinical phenomena and their mechanisms The influence of the schools of physiology and experimental pathology will continue to work in that direction But I greatly fear that the very complexity of these phenomena is withdrawing interest from the planned study of their causative diseases To that extent there is a growth of ignorance about these diseases The tempo of events in some diseases may be so slow that they will be accurately observed only by a general practitioner, or by a family doctor over a period of many years, or the disease may be so uncommon, and its distribution so wide, that special arrangements may be required to gather a sufficient number of examples within the reach of the observers Hospitals as we know them will not be the best places from which this work can be organised If clinical research is to be used to get a full picture of disease, it must equip itself to carry the observations beyond the hospitals and extend the searches which can best be done in family practice and by field survey of random samples of population The methodology of planned clinical observation in family practice and in random samples of the population will become a responsibility of medical schools

I foresee the day when medical faculties of universities will have three provinces of clinical training and clinical research One will be in hospitals, where training and the research will be dependent on the facilities which remain after the demand for specialist forms of treatment have been satisfied. The second province will be a sample of population in their own homes which can be provided in family practice The third will be in expeditions to communities, whether they be in a mining village, a Hebridean island, a Chesterfield Islet, or wherever the inquiry takes them If we are not too pompous about it all, if we can escape the dead hand of dull conformity, if we can get the freedom to make experiments in arranging our institutions, if we can recover the initiative to make the experiments—then our medical schools and teaching hospitals may take on this work. If they fail it is difficult to see how else it can be done.

RENAL FACTORS IN THE PRODUCTION OF HYPERTENSION *

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Nature of the Extrarenal Factor

IT is tempting to speculate that the kidneys and adrenals form part of a homœostatic mechanism which, through the control of tissue electrolytes, maintains arteriolar tone and adapts the blood pressure to changes in the internal environment This must remain an imaginative concept until the specific rôles of the kidney and adrenal in relation to normal and high blood pressure have been determined How far does the availab evidence shed any further light on this problem? In the first place, it must be emphasised that experimental studies have proved only that the various forms of hyper tension associated with renal ischæmia or total nep tomy cannot be sustained (I use this word deliberatel since there may still be some doubt about the in development of hypertension) in the absence of adr cortical tissue , and further that salt and deoxy acetate can, within the time limits of the experiments provide a fairly effective substitute for the adrenal corte in this respect

It may be argued on the one hand that the adren cortex or its substitutes merely provide the physiolo conditions necessary for the maintenance of tone, whether normal or abnormal, and that conditions form an essential background for any hy tensive process, renal or extrarenal In this case hypertension could arise from some pressor mech independent of the adrenal cortex, acting directly on th peripheral arterioles This is the one alternative the other hand, renal and renoprival hypertension ma both result from a direct dislocation of some form adrenal electrolyte control of arteriolar tone

If we could decide between these alternatives we sh have taken an important step forward in und the factors responsible for renal hypertension Th are many observations which favour the second hy thesis of a direct connection between the kidney and adrenal-electrolyte mechanism

Although variations of salt intake have little effect the normal blood-pressure until gross disturbance of b tor has been produced there is considerable evidence hich I summarised in my first lecture that experimental nal hypertension in animals is aggravated by addition salt to the diet and can be reduced by withdrawing salt nversely, hypertension can be more readily produced both salt and deoxycortone acetate if the kidneys are maged or if one kidney is removed These experiments ggest that there is a mutual potentiation between the pertensive effects of renal damage on the one hand d salt and deoxycortone acetate on the other Never less somewhat similar relationships hold for other essor agents and the facts would not be inconsistent ith the theory that there are two unrelated mechanisms ting independently on the peripheral arterioles.

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* The second Oliver Sharpey lecture for 1953, delivered the Royal College of Physicians of London on March The first lecture appeared in last week's issue

In the second place there is reliable evidence that anges in tissue-electrolyte distribution occur in experi ental renal hypertension Eichelberger (1943) observed increase in extracellular fluid of muscle tissue in dogs ith renal hypertension. Laramore and Grollman 950) found a rise in the percentage sodium content and fall in potassium in the heart-muscle of hypertensive ts. Ledingham (unpublished work) has recently monstrated a significantly raised extracellular fluid lume in heart-muscle in rats with experimental renal pertension this is part of a generalised body increase o. the rise in sodium and fall in potassium are plained by a gain in extracellular fluid It is found at this gradually returns to normal over a period of ree months despite persistence of the hypertension dministration of deoxycortone acetate to normal rats so produces an increase in extracellular fluid Whilst is evidence supports the view that the adrenal regu tion of tissue electrolytes is disturbed in the early ages of experimental renal hypertension it seems robable that this is the result rather than the cause the hypertension.

We need in fact some direct evidence of an excess of drenal pressor factor in the body when the blood ressure changes from normal to hypertensive levels.

The only evidence of this nature of which I am aware derived from the experiment I mentioned in my first cture which demonstrated the effect of adrenalectomy n renoprival hypertension in the parabiotic rat. Return g to this experiment, it will be recalled that bilateral drenalectomy alone in one member of a parabiotic pair roduces no fall in blood pressure but that the same peration reduces to the normal level the hypertension roduced by bilateral nephrectomy Fig 7 represents hese observations diagrammatically

1 Bilateral nephrectomy in rat B produces hypertension ut the blood pressure of A remains normal. An extrarenal essor factor is therefore operating in B which for some eason is unable to affect its partner The most likely xplanation is that the rate of transmission of this factor cross the union is slower than the rate of its inactivation or limination by the kidneys of A.

2. Bilateral adrenalectomy in the nephrectomised rat B educes the renoprival hypertension to normal—i.e., the extra enal factor depends on the presence of adrenal-gland tissue. It is notable that the blood pressure does not fall elow normal as occurs after the same procedure in the ingle rat.)

3 Bilateral adrenalectomy alone in rat B produces no fall n blood pressure as it does in the single rat

From this experiment we infer that after total adrenal ctomy a parabiotic rat by virtue of its vascular union ith a normal partner is able to maintain normal blood ressure but cannot maintain renoprival hypertension Ience it follows that in the hypertensive rat the adrenals nust, in terms of pressor activity be functioning at a igher level than normal or alternatively the adrenal ressor factor is being produced at the normal rate but is ccumulating in the nephrectomised rat owing to the bsence of some renal inactivating mechanism Grollman nd his colleagues (1940) reported that although bilateral

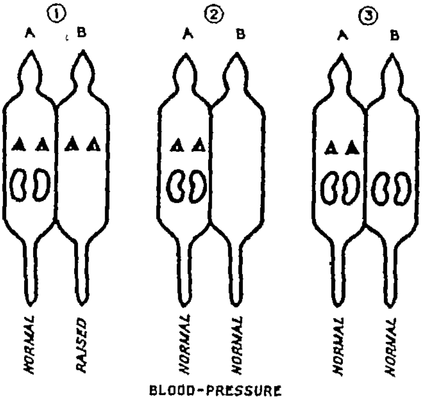

Fig 7—Effect of (1) nephrectomy (2) nephrectomy and adrenalectomy and (3) adrenalectomy alone on the blood-pressure of one member of a parabiotic pair of rats

nephrectomy produced hypertension in dogs whose survival time was prolonged by use of the artificial kidney, no rise in blood pressure occurred if under the same circumstances one kidney was excised and the ureter of the opposite kidney was transplanted into the duodenum or the vena cava—i.e., the presence of non excreting renal tissue apparently inactivated the extrarenal mechanism Assuming that the failure of blood pressure to rise in this second experiment was not due to postoperative shock or some related cause these findings support the theory that normal kidney tissue inactivates the adrenal factor and that after total nephrectomy hypertension is due to the cumulative effect of this factor

If this hypothesis is correct it is essential to find an explanation for the observation that hypertension can be produced by unilateral renal damage without disturbing the opposite kidney It would be necessary to postulate that the production of renal ischæmia in one kidney induced a functional change in the opposite kidney which prevented it from inactivating the adrenal factor In my first lecture I recounted experiments which showed that when hypertension has been present for some time the opposite kidney undergoes a change which enables it to sustain hypertension after removal of the ischæmic kidney This effect is not observed in all hypertensive rats and could not in any case operate until hypertension was established. There is some evidence however that the production of acute ischæmia in one kidney may produce an immediate vascular disturbance in the opposite kidney Gordon and Flasher (1951) have recently observed that after one renal artery of the rabbit had been clamped for five to fifteen minutes, release of the clamp was followed by blanching of the opposite kidney and this phenomenon was shown to be due to a non pressor humoral factor There is therefore some reason to believe that both kidneys are implicated when hypertension is induced by constricting one renal artery More evidence on these lines is essential if renal and renoprival hypertension are to be explained on the unitary hypothesis outlined above

I have so far discussed the rôle of the adrenals on the assumption that some active principle resembling the salt hormone is involved. It is possible that other adrenal steroids may also play a part. Cortisone is known to produce hypertension under certain conditions. Ledingham has reported experiments which show that cortisone can effectively take the place of the adrenals in the maintenance of renal ischæmia hypertension. He has also demonstrated that in adrenalectomised rats the pressor effects of deoxycortone acetate and cortisone have different time relations but are summated when both substances are administered.

We have therefore a variety of evidence which is consistent with the hypothesis of a direct relationship between the kidney and the adrenal electrolyte mechanism in experimental renal hypertension. Lacking more direct proof, such as might be derived, for example, from estimation of cortical steroids in the blood, this hypothesis remains a tentative one; but I believe it provides a new stimulus and opportunity for further investigation. Much of the information has been obtained from experiments on rats subjected to conditions far removed from the physiological state. Nevertheless similar experiments in other animals by many investigators have shown that, although there are definite species differences in response, the same factors seem to be involved in the production of experimental hypertension. There is still some uncertainty whether this mechanism operates in the same manner during the initial development of high blood pressure as it appears to act in chronic hypertension; that again is a subject for future investigation. If from these experiments a reasonable presumption is established that renal hypertension is maintained through some action of the kidney on an adrenal cortical hormone, and that this in turn acts through the influence of tissue electrolyte distribution on arteriolar tone, we have taken the first step towards an understanding of the physiological mechanisms involved in renal hypertension.

Kidney Lesions and Hypertension

I have already referred to the fact that of all the types of renal manipulation which have been used to produce experimental hypertension, constriction of the renal artery is the most effective. High blood-pressure results from a wide variety of structural lesions of the kidney, and it has been with reason assumed that the common operative factor is circulatory impairment analogous to that produced by clamping a renal artery. Since the normal renal blood flow is very large—equivalent to one third of the heart's output—and since the specialised arterial system of the kidney is seriously affected in most forms of renal damage, it is no difficult matter to find an adequate morphological basis for renal hypertension in kidney disease. It was, however, of particular interest when it was discovered that in the rat the development of hypertension could itself lead to severe secondary arterial lesions in the kidney, and that these changes were associated with structural damage to the renal parenchyma which closely resembled in gross and in detail the histological picture of malignant nephrosclerosis in man. Following our original observations several groups of other workers have confirmed these findings in both the rat and the rabbit (Friedman et al. 1941, Schroeder and Neumann 1942, Patton et al. 1943, Flasher et al. 1951). In some of this work the interpretation of the histological changes has been complicated by the occurrence of spontaneous renal lesions and by a failure to distinguish between vascular damage produced by clamping the kidney and acute hypertensive lesions. Goldblatt (1948) held the view that the lesions we reported were due to spontaneously occurring pyelonephritis. Apart from the fact that this condition does not occur in our rat colony the controlled nature of the experiment completely rules out this possibility. Working on an entirely new series of animals Floyer (1951) has confirmed in every detail our original observations. A further argument maintained by Goldblatt is that the lesions are not attributable to hypertension alone but renal failure in some form is necessary for their development. Byrom and Dodson (1948) have answered this criticism by demonstrating the production of rena arteriolar necrosis—which is the essential lesion—whe the blood-pressure was suddenly raised by direct intra arterial injection of saline. It is of interest also tha arterial necroses commonly occur in the viscera of th parabiotic rat in which severe hypertension has bee produced by total nephrectomy, but not in its partner i which the blood pressure has remained normal (Ledingham 1951). A certain amount of confusion has aris from reports that similar lesions are found in dogs in th absence of hypertension following injection of rena extracts and in experimentally produced uræmia followin bilateral ligature of the renal arteries. Vascular necrose after injections of renal extracts are most probably th result of an allergic reaction. In experimental uræmia the severe tissue necroses in the heart and other viscera are of a different character from those produced b hypertension.

That hypertension can give rise to acute arterial necroses in the kidney and other organs is therefore wel substantiated. Why in the same experiment some animals develop these vascular lesions, whilst other with a similar degree and duration of hypertension do not, is still a mystery. I am of the opinion that a sudden rise in blood-pressure to a high level will produce the lesions in most rats; but in animals, as in humans, we must recognise an individual variation in susceptibility.

I described in my first lecture recent experiments which provided additional evidence for our original thesis that the opposite ("untouched") kidney is responsible for the hypertension which persists after removal of the ischæmic kidney. Many months after this operation we observed acute vascular lesions in the remaining kidney and inferred therefore that hypertension perpetuates itself through the production of some change in the kidney, associated with these vascular lesions. This concept of the vicious circle was a natural corollary of the dual proposition that, on the one hand, renal vascular occlusion gives rise to hypertension, and that, on the other, hypertension leads to occlusive vascular lesions.

Application of Experimental Results

The principal difficulty in judging the possible clinic implications of all this experimental work arises from th impracticability of repeating these various unphysiological investigations in man. The main recent developments in the experimental approach to human renal physiology concern clearance techniques; these have given us new and more accurate information about functional disturbances in kidney disease, but no fresh light has been thrown by them on the ætiology of either renal or essential hypertension. Deviations from normal clearance appear more likely to be the consequence than the cause of high blood pressure, and in any event the results of such tests are not appreciably altered when experimental hypertension is produced in animals by renal artery constriction.

Of the three aspects of experimental investigation which I have considered, the first, concerning the search for a renal pressor agent, does not appear in the present state of our knowledge to carry any clinical implications. In the second field, which has involved us in the problems of hormone activity, we are still probing uncertainly among the fundamental issues; here is undoubtedly a sphere of application, but so far filled only with likely intangibles. I shall hope to say a little of these later. The most useful contribution to our understanding of the problems of hypertension in man has been derived from the third experimental topic—the anatomical studies which I have just described. This subject was discussed in detail by Sir Arthur Ellis in his Croonian lectures of 1942. The conclusions he presented then have withsto the test of experience, and I shall refer to some of the briefly, in order to comment on more recent work and on points of interpretation which merit further emphasis

RENAL HYPERTENSION

I will deal first with certain problems of high blood pressure in primary disease of the kidneys, in particular chronic nephritis and unilateral renal disease.

Type I Nephritis

There are obvious morphological changes in type I nephritis which would offer an ideal setting for renal ischæmia hypertension In acute nephritis the diffuse inflammation of the glomeruli, the characteristic epithelial crescent formation of its rapidly progressive course and the generalised reduction in the parenchyma in the more chronic cases might well reproduce an impairment of the circulation analogous to renal-artery constriction There is, however one course of chronic nephritis, which Volhard designated the 'vascular type' in which an additional factor appears to operate When the disease runs this course the patient continues for many years, sometimes for decades with slight to moderate hypertension and with no impairment of renal function; eventually the blood pressure rises steeply often over the course of a few months and becomes fixed at a high level with the subsequent development in many instances of the malignant termination characterised by papillœdema encephalopathy, cardiac asthma and renal failure There is no clinical evidence of recurrence or reactivation of the nephritis to account for this change in the course of the disease, and the histological picture at various stages of the hypertensive transformation shows no vestige of a renewed activity of the glomerulonephritis in its place we see wedge shaped areas of renal atrophy with glomerular interstitial and vascular lesions closely resembling those produced by hypertension in the experimental animal. Corresponding to the later and more rapid clinical progression vascular damage becomes more pronounced, and acute necrotising changes in arterioles and glomeruli are superimposed on chronic organised lesions There is a very strong presumption that secondary hypertensive lesions in the kidneys are responsible for this transformation and that the vicious circle operating slowly at first and then with increasing tempo plays a decisive rôle in the natural history of this common form of Bright's disease.

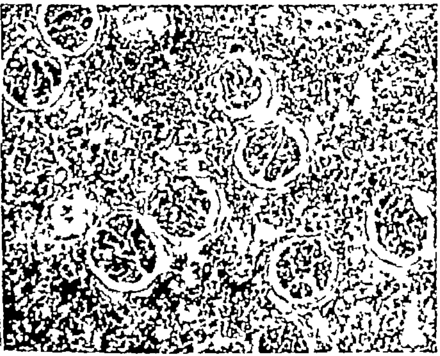

Fig. 8—Chronic ischæmic changes in area of kidney supplied by thrombosed renal artery (hæmatoxylin and eosin. × 83)

Type-II Nephritis

In chronic type II nephritis the clinical and [illegible] features suggest a different sequence. There are many patients chiefly women and children, in whom the disease runs a long course with no considerable degree of high blood pressure But the commonly observed duration of the disease in men particularly, is from three to six years and in its later phases at least, hypertension is prominent A malignant termination is observed in more than half the cases. Hypertensive vascular lesions, acute or chronic are inconspicuous in the kidneys, but the anatomical changes in the glomeruli (and they are the most constant and easily recognisable in the whole of Bright's disease) indicate an insidious disorganisation of the capillaries. The progressive, relatively rapid course of this disorder and its prominent hypertensive features could well be attributed to the circulatory restriction produced by its characteristic glomerular lesion

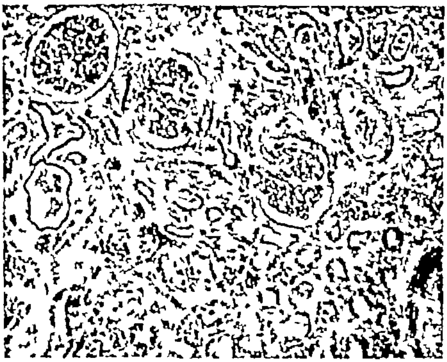

Fig. 9—Endarteritis and glomerular necrosis in section from lower pole of same kidney (hæmatoxylin and eosin. × 83)

Unilateral Renal Disease

The discovery that in the rat sustained hypertension could be readily induced by constriction of one renal artery had an obvious relevance to the recognised association of high blood pressure with unilateral renal disease in man The further observation that removal of the ischæmic kidney more often than not failed to abolish the hypertension has also a parallel in the human disease. It is now generally appreciated that only in

Fig. 1—Necrosis of afferent

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exceptional cases will unilateral nephrectomy reduce the blood-pressure completely and permanently to normal

Whether this persistence of hypertension in man after unilateral nephrectomy can in some cases be attributed to secondary hypertensive changes in the opposite kidney cannot be proved, but there is no doubt that such lesions commonly occur The combination of one contracted kidney with a large opposite kidney, which shows on microscopic examination the picture of malignant nephrosclerosis, is now familiar to most morbid anatomists I have recently encountered such a case of unusual interest

The patient presented with the clinical features of malignant hypertension, and there was a past history of an attack of hæmaturia

Post mortem examination revealed a remarkable picture A main renal artery on the right side was occluded by an *organised thrombus, and the major portion of the kidney was* flabby and congested The lower pole, however, showed on section an entirely different appearance, which was similar to that of the opposite kidney Histologically the upper part of the right kidney showed slight ischæmic scarring such as may be seen in the clamped kidney of the hypertensive rat (fig 8) The lower pole of this kidney and the whole of the opposite kidney, on the other hand, showed gross changes of malignant hypertension with endarteritis, arteriolar necroses, and acute and chronic hypertensive lesions in the glomeruli (figs 9 and 10)

This case provides plain and convincing anatomical evidence that the hypertensive changes followed the production of a renal ischæmic lesion in one kidney The remarkable similarity between the sequence of events, both anatomical and functional, in such instances and in the rat with induced hypertension provides an acceptable assurance of the validity of our experimental method. A number of papers have recently appeared claiming that the incidence of hypertension in patients with unilateral renal disease is no greater than in the general population This may well be, but it does not alter the fact that severe hypertension, sometimes with malignant features, is occasionally encountered in patients with a single contracted kidney, nor should such statistical generalisations be accepted as an argument against nephrectomy, since this may be a life-saving measure The lesion in such cases is commonly a developmental anomaly complicated by chronic pyelonephritis

ESSENTIAL HYPERTENSION

Malignant Essential Hypertension

The observation by Wilson and Byrom (1939) that, in the rat, the histological changes of malignant nephrosclerosis appeared in the untouched kidney, but were absent from the clamped kidney, provided experimental evidence for accepting the "malignant hypertension" of Volhard as a form of essential hypertension rather than as a variety of chronic nephritis It established the fact that nephrosclerosis was a sequel of the hypertension and not its cause, and demonstrated the ischæmic basis of this typically inflammatory renal lesion It explained the severe and progressive course of malignant hypertension and the confusing similarity, both clinical and histological, of the various forms of hypertensive Bright's disease in their late stages

Although the vascular lesions of nephrosclerosis are not the primary cause of the hypertension they may perpetuate and aggravate it by progressively increasing the renal ischæmia We nowadays see patients with this disease in its earlier stages, during the period of development of the malignant features From observations we have recently made on the clinical course, and from renal biopsy studies in patients submitted to sympathectomy, it is apparent that at its onset malignant hypertension is often an intermittent disorder Phases of increased blood pressure may produce papillœdema or encephalopathy which subside during quiescent periods Histologically, active and healed stages of the vascular lesi are found corresponding to the clinical phases Eventua the condition becomes fixed, papillœdema fails to regre and the disease advances with increasing speed might be argued that the primary cause of the increa peripheral resistance in malignant hypertension is first phasic, then continuous, with a terminal rise activity , but the *natural history is more aptly account* for by the vicious circle based on perpetuation a aggravation of the hypertension by secondary h tensive vascular lesions

The natural progress of the various types of hyp tensive Bright's disease *to a malignant terminati* illustrates the desirability of attempting to break vicious circle in the early stages before serious irreversible changes develop in the heart, brain, kidneys The observed fact that reduction of blo pressure by sympathectomy, hexamethonium drugs, non-specific operations—even though this reduction only partial—can retard the progress of the disease *an added argument for the existence of the vicious circ* for these measures do not act on the fundamental cau of the high blood pressure but only modify the con of the disorder by a non specific effect on the level of t hypertension and thereby on its consequences

It is now generally recognised that the clinical ma festations of malignant hypertension, of which papi œdema is the certain diagnostic sign, may occur as sequel to benign hypertension, to the various forms renal hypertension, and occasionally to other rare for of hypertension of endocrine origin—e g , phæochrom cytoma and Cushing's syndrome The term "maligna hypertension" is used by some writers to indicate t clinical syndrome, and by others in the original connot tion used by Volhard to denote the malignant form essential hypertension in contrast to benign hypertensio This dual usage is unfortunate since it tends to obsc again the issue which experimental work has clarifie *It is at the present time particularly unhappy* since the is still a lingering prejudice that essential hypertensio whether benign or malignant, may be due to orga renal arteriolar disease Confusion will be avoided if patients with the picture of malignant hypertension search diligently for the primary cause—whether it chronic nephritis, unilateral renal disease, adren tumour, or essential hypertension , and if, having *fou* the cause, which is not difficult in the great majori of patients, we use the appropriate diagnostic term *designate a case of* pyelonephritis as malignant hyp tension is no less inappropriate than to attach diagnostic label "nephrotic syndrome" to the dise we now recognise as diabetic glomerulosclerosis I emph sise this point since confusion in terminology has *be* the bane of Bright's disease and is largely responsi for the attitude of defeatism which often prevents o recognising obvious disorders of function and *sometim* deprives the patient of urgent and effective treatment

If, then, malignant hypertension may develop in a patient with high blood-pressure, what is the fundament difference in mechanism from the more common beni form, and does the kidney play any rôle in its *develo* ment ? I am sure it is now clearly understood th although the acute destructive vascular lesions which a diagnostic of malignant hypertension may accentua the disorder they cannot play any part in its origi There is so far no evidence of any anatomical basis f the change from the benign to the malignant typ Nevertheless the attitude that the difference is pure a matter of degree or severity is unsatisfying Very hi levels of blood-pressure may long persist in experimen animals and in man with no sign of the maligna features which similar levels rapidly produce in oth individuals, and yet, as Volhard pointed out, *th* *Umschlag*, or malignant transition, may eventually oc

Figs. 11 12, and 13 (by courtesy of Dr F B. Byrom)—Consecutive photographs of dorsal surface of right parietal lobe of living rat as seen through a Perspex window (× 25) Branches of the middle cerebral artery enter the field from below (marked with arrows) Hypertension induced by removal of right kidney and constriction of left renal artery

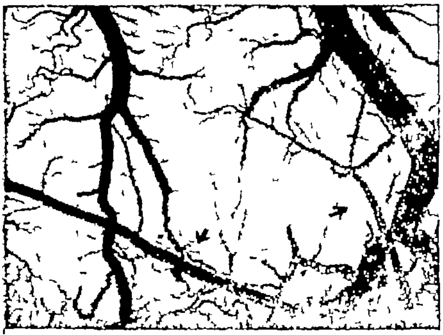

Fig. 11—Hypertension without cerebral symptoms. Blood-pressure 195 mm. Hg The vessels show the same appearance as in the normotensive rat.

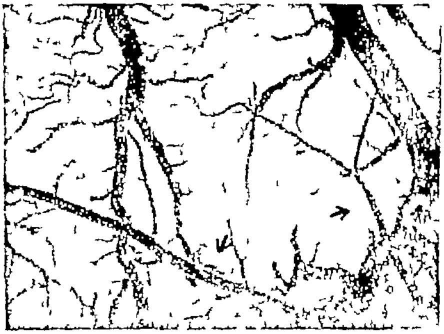

Fig 13—Two months after abolition of hypertension by removal of clip. Blood-pressure 130 mm. Hg ; animal in normal health. Vessels appear normal

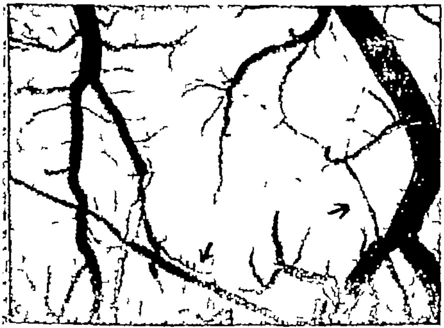

Fig 12—Two months later photograph fifteen minutes after onset of generalised convulsions. Blood-pressure 223 mm. Hg Intense spasm of branches of middle cerebral artery The clip was now removed from the renal artery

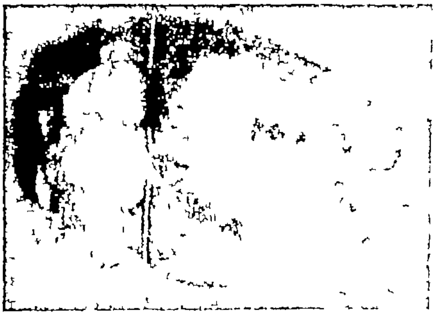

Fig 14 (by courtesy of Dr F B. Byrom)—Brain from rat with hypertensive encephalopathy photographed thirty minutes after injection of trypan-blue showing scattered focal staining in cerebral cortex.

after a decade or more of the benign course. From a combined study of the clinical and histological manifestations of the syndrome I think there is some intimation of a possible difference in ætiology between the early or fulminating syndrome of malignant hypertension and the delayed or chronic type The best approach to this problem is by comparison of the incidence of the malignant termination in renal and in essential hypertension. Kimmelstiel and Wilson (1936) studied the clinical and histological features in 250 consecutive cases of essential hypertension submitted to post mortem examination 4% of the series were clinically and histologically diagnosed as malignant essential hypertension, and less than 1% were of the transitional type representing a malignant termination to a long standing benign hypertension. In renal hypertension on the other hand the incidence of the malignant syndrome is quite different as the following figures show :

	Total cases	*Malignant hypertension syndrome*
Type-I nephritis rapidly progressive	13	4
Type-I nephritis slowly progressive	65	32
Type II nephritis	41	26
	119	62

In this series of cases of chronic nephritis studied in the renal clinic at the London Hospital there were 78 cases of progressive type I nephritis (confirmed histologically) and 41 of progressive type II nephritis 36 in the first group and 26 in the second developed the malignant hypertensive termination—i.e. an incidence of over 50% in the whole series This is of the same order as the incidence of malignant nephrosclerosis in rats with experimental renal hypertension It is apparent that in organic renal disease the malignant termination is a fairly general hazard and is presumably related to the steadily increasing severity of the hypertension associated with progressive renal damage a similar explanation may possibly apply to the small transitional group in which a malignant termination is superimposed on a long-standing benign course for the kidneys in these patients show severe ischæmic scarring But such a background of organic renal disease plays no part in the usual development of the malignant type of essential hypertension. Whilst some of these patients are known to have had benign hypertension for a considerable period in others it is certain that the high blood pressure is of recent origin moreover histologically, chronic ischæmic changes in the kidney may be inconspicuous or even absent I do not think we can escape the con clusion that there is some special disorder of function in those patients with essential hypertension who develop the malignant termination early in the disease This may be in the nature of an abnormally intense response of the arterioles to the pressor mechanism or an excessive activity of the pressor mechanism itself, there is at present no evidence that the kidney plays a primary rôle in this fundamental disorder

Hypertensive Encephalopathy

I cannot leave this subject without brief comment on hypertensive encephalopathy This symptom complex of disorientation, convulsions, amaurosis, and coma occurs in acute nephritis, in eclampsia, and in any form of chronic Bright's disease complicated by the syndrome of malignant hypertension From a study of encephalopathy in acute nephritis, Volhard recognised that renal failure played no part in its development, and for this reason applied to it the term pseudo-uræmia The experimental verification of this conclusion was apparent when in rats with hypertension due to unilateral renal artery constriction we observed the typical syndrome of hypertensive encephalopathy and noted its prompt relief when the hypertension was abolished by excision of the ischæmic kidney Encephalopathy in man, in either acute or chronic hypertensive states, can be similarly relieved by measures which lower the blood-pressure There has been some difference of opinion whether this complication is a result of excessive cerebral vasoconstriction or of cerebral œdema Hypertensive encephalopathy occurred in 11 of our series of acute nephritis (a 6% incidence) In 6 of these patients the cerebrospinal fluid pressure was measured, and in 4 it was normal Furthermore a rise in blood pressure is occasionally observed just before an attack—an observation which favours vascular spasm Dr F B Byrom has recently carried out some fundamental, and I believe decisive, investigations on the underlying mechanism By the introduction of transparent windows into the skull of the rat he has obtained many photographs of the superficial cerebral arteries before and during attacks of encephalopathy He has kindly sent me an account of this as yet unpublished work, and serial photographs (figs 11–13) which demonstrate convincingly the occurrence of cerebral arterial spasm This phenomenon was observed in 57 out of 65 rats with hypertensive encephalopathy In rats with severe hypertension but no cerebral symptoms (148 observations on 88 animals) no spasm was recorded Very occasionally localised ballooning of larger arteries occurred during the attack These experiments are not yet completed, since it is essential to exclude the possibility that some of the changes observed may be artefacts related to the presence of a cranial window in an animal with an expanding brain and irritable hypertensive arteries Nevertheless Byrom draws two firm conclusions first, that the view that the cerebral arteries are too thin-walled to be capable of spasm is no longer tenable, at least as far as the hypertensive rat is concerned, and, secondly, that the irritability of the cerebral arteries is remarkably increased in encephalopathy Organic lesions in the brain were not a necessary accompaniment of encephalopathy and were absent in half the cases, nevertheless arteriolar necroses were frequently found, and it may be that these resulted from excessive vascular spasm or from a resulting paralytic dilatation General cerebral œdema was a late development but vital staining with trypan blue showed local areas of increased capillary permeability and œdema in the cerebral cortex (fig 14) Hypertensive encephalopathy in the rat is reversible to a remarkable degree If the hypertension is abolished by removing the clip from the renal artery the symptoms are promptly relieved, the spasm relaxes, and the cerebral œdema is quickly dispersed Whilst I am not suggesting that any specific renal factor is involved in the production of hypertensive encephalopathy, I Byrom's observations provide another striking of the similarity of hypertensive behaviour in the and in man

Benign Hypertension

In this, the common form of essential hyp as Clifford Allbutt discovered by clinical obse over fifty years ago, involvement of the kidney, in far as the patient is concerned, is of no great There is no evidence that structural changes in arteries or arterioles play any part in the genesis of hypertension, nor in the great majority of cases such changes influence the course of the disease may be that functional vasoconstriction, stimulated b some extrarenal factor, provides a renal mechanism the hypertension, but again there is no evidence for hypothesis Returning to our second topic of experi mental investigation, the possibility that the adren cortex plays a rôle in renal hypertension at once the question of a similar participation in hypertension Elevation of the blood-pressure Cushing's syndrome, which closely resembles hypertension and may develop the malignant term tion, is apparently the result of adrenal cortical over activity Low blood pressure is a diagnostic feature o adrenal cortical failure in Addison's disease, and sub stitution therapy by deoxycortone acetate occasionall leads to hypertension in the course of treatment S restriction is undoubtedly effective in lowering blood-pressure in some cases of essential hypertension. These are the intimations, promising yet intangible, which I have previously referred They may yet lead to the discovery of a common metabolic process underly ing most, if not all, forms of hypertension If there is such a final common pathway I believe it may us also to the method of regulation of the no blood-pressure

I am greatly indebted to my colleagues, first Dr F B Byrom and later Dr J M Ledingham and Dr M A Floyer, who have made a large contribution, both practical and critical to these studies Fig 5 is taken from an article by Dr Ledingham in *Clinical Science* (1951, 10, 423), and fig 6 an article by myself in the *British Medical Bulletin* (1952, 8 316) and I am grateful to the editors of these journals f permission to reproduce the figures

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CLINICAL PATTERN OF CHRONIC BRONCHITIS

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BRONCHITIS especially chronic bronchitis has been an xceedingly popular diagnosis in the British Isles ever ince the term was introduced to medical literature by Badham (1808) During the past century improved methods of investigation have enabled clinicians to place many patients having cough sputum and breathlessness as their predominant symptoms into other diagnostic ategories but there remain many for whom no more ppropriate diagnosis than chronic bronchitis is forthcoming

With a view to establishing some basic facts concerning his rather heterogeneous group a questionnaire has been completed upon 1000 adult bronchitic patients during the period January 1951 to January 1953 The great majority were seen in a special bronchitis clinic held weekly at the Brompton Hospital for this purpose The others were seen at St Bartholomew's, and a few n private practice There was no selection except that he Brompton patients included 362 civil servants who nd had repeated spells of sickness recorded as 'bronchitis' and were referred by the Treasury medical department for an opinion The questionnaire was completed at the Brompton by one of us or the Treasury medical officer and at St Bartholomew's by one of us or his chief assistant. All were checked by at least one of us. The forms were designed so that they could be completed t a single visit to an outpatient clinic about half an hour eing taken for each patient.

Only patients aged 20 or more at the time of interview were included All had chronic bronchitis in the sense in which the term is usually applied—i.e, they had a disease which appeared to be predominantly affecting their bronchi and having cough, sputum and breathlessness as its outstanding symptoms without evidence of any other important primary or precipitating disease of the respiratory or cardiovascular system or other part of the body They all had some degree of disability from either breathlessness or infection or both and the symptoms had persisted, not necessarily continuously for at least a year Each of the 1000 patients underwent physical and radiological examination Some difficulty was experienced in determining the common usage of the term chronic bronchitis' as opposed to asthma Asthma was taken to mean periodic attacks of breathlessness with a feeling of tightness in the chest and difficult expiration No such patients were included unless they gave a clear history of bronchitis before the onset of such attacks

The age-distribution of the 1000 patients shown in table I may be taken as fairly representing that at which this type of patient seeks advice from hospitals in London

TABLE I—DISTRIBUTION BY AGE AND SEX OF 1000 PATIENTS WITH CHRONIC BRONCHITIS

Age (yr)	Males	Females
20–29	23	22
30–39	60	34
40–49	135	53
50–59	353	47
60–69	[illegible]	21
70 or more	[illegible]	3
Total	820	180

The highest incidence is in the sixth decade, a time at which breathlessness often tends to become troublesome

No firm conclusions can be drawn about the distribution by sex Males predominate in a ratio of 4 6 to 1 but even if the civil servants of whom 331 out of 362 were males, are excluded, the ratio of men to women is still 3 3 to 1 The significance of these figures is doubtful since many women were excluded because they had asthma rather than bronchitis also men probably seek advice from hospital earlier than women especially if they are losing time from work. Housewives can often adjust their lives, in respect of work and exposure to adverse climatic conditions, sufficiently to enable them to do their work without undue breathlessness or distress whereas men cannot avoid unfavourable weather and adverse factors at work

In addition to the 1000 bronchitic patients, relevant parts of the questionnaire were completed upon 300 controls of similar age sex and social status The controls were derived from a medical outpatient clinic and from the general surgical wards at St Bartholomew's care being taken to exclude patients who had any pulmonary disease the forms were completed by one of us and his chief assistant.

The analysis fell into two parts

(1) A comparison between 300 patients with chronic bronchitis and 300 comparable controls in relation to family history, respiratory disorders of childhood, allergic diseases, colds in the head smoking habits, and blood pressure

(2) A review of 1000 patients with chronic bronchitis for age and mode of onset age of onset of breathlessness, degree of breathlessness character of sputum clinical severity radiological findings, effect of climate occupation, and living conditions.

Patients Compared with Controls

Age-distribution

Table II shows the distribution by age and sex of 300 controls The relatively large numbers in the younger age groups, compared with the 1000 patients

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TABLE II—DISTRIBUTION BY AGE AND SEX OF 300 CONTROLS

Age (yr)	Males	Females
20–29	23	1
30–39	52	3
40–49	80	12
50–59	71	12
60–69	31	6
70 or more	7	2
Total	264	36

300 of the 1000 patients with chronic bronchitis of similar age and sex are compared with these

is due to the difficulty of finding older men and women free enough from respiratory symptoms to act as controls

History of Bronchitis in Relations

Relations being defined as fathers, mothers, brothers, half-brothers, sisters, half sisters, sons, or daughters, the 300 patients had 2248 relations, of whom 256 (11 4%) had chronic bronchitis, whereas of 2137 relations of controls only 82 (3 8%) had chronic bronchitis This difference is statistically significant and is of the order to be expected from clinical impressions, but possibly bronchitic patients are more likely to remember bronchitis in relations than are other people , therefore some allowance should be made for this The 1000 patients had 7786 relations, of whom 803 (10 3%) had bronchitis , this figure may be regarded as reasonably accurate for the hospital class of patient in London

Among the relations of the 300 patients, 677 had died, and in 90 (13 3%) of these bronchitis was considered to be at least a contributory cause of death , the figures for controls were 644 deaths, to which bronchitis at least contributed in 24 (3 7%) The significance of these figures depends on the validity of history-taking , certainly the great apprehension of many bronchitic patients about the outcome of their disease was impressive Bronchitis leads to complications in the lungs and heart and, though it may often not progress very far, it is associated with death in a high proportion of the near relations of patients who have it

A history of allergic disorders was sought among the relations Of the 2248 relations of patients 57 (2 5%) had asthma, 8 (0 4%) hay-fever, and 11 (0 5%) eczema The corresponding figures for 2137 relations of controls were 31 (1 5%) with asthma, 9 (0 4%) with hay-fever, and 6 (0 3%) with eczema No reliable figures could be obtained for migraine or for urticaria

TABLE III—TIME LOST FROM SCHOOL AS A RESULT OF RESPIRATORY INFECTIONS IN 300 PATIENTS WITH CHRONIC BRONCHITIS AND CONTROLS AT OR BEFORE THE AGE OF 12

Time lost	Bronchitic patients	Controls
Nil	221 (*73 7%*)	281 (*93 7%*)
Occasional week	46 (*15 3%*)	16 (*5 3%*)
Habitual absentees	19 (*6 3%*)	2 (*0 7%*)
Total absence of more than 1 year	14 (*4 7%*)	1 (*0 3%*)
Total	300	300

Childhood Illnesses

Table III shows that chronic or recurring respiratory infections were much commoner in patients than in controls The greater differences are seen in the longer absences from school but even absences of an occasional week were greater in patients than in controls By contrast, 73 7% of the patients lost no appreciable amount of time from school through respiratory infections

Bronchitis and pneumonia were by far the commonest serious respiratory infections in childhood in those who subsequently developed bronchitis, and occurred much more often than in the controls Of the patients 67 (22 3%) gave a history of bronchitis in childhood 43 (14 3%) of pneumonia The corresponding f for controls were 7 (2 3%) and 18 (6 0%)

Relationship of Colds in the Head to Bronchitis

The annual mean number of colds among the p was 2 6 and among the controls 1 6 Table IV shows frequency with which colds "went down to the Very few of the patients did not have colds in the and 90% of them stated that they "went down to chest" Colds "went down to the chest" in 27% the controls but did not produce any real disability

Occupational Factors

The predominant occupation of each patient control at ages 15–25, 25–35, and more than 35 was no Table V shows the occupation by the Minister of Lab code at the ages 15–25 for the 300 patients controls, the distribution being similar in each except for a slight preponderance of clerical workers the controls The proportions in the five grades remained similar for patients and controls in of the three age groups noted Both patients controls aged 15–25 were equally distributed light and heavy work, and between indoor and occupations At ages over 35 almost three as many were doing light as were doing work, and the same proportion were working but there was no significant difference in either between the patients and the controls This might first sight appear anomalous, in view of the disa symptoms of chronic bronchitis, but is explained pa by the fact that half the patients were normally emp in light work, largely clerical, which they were able manage provided they were fit for a measure of ment For the rest, the difficulties of learning a trade after the age of 35 are well known, and there a natural tendency for the unskilled and semi to become skilled, thus lightening the amount of he work which might otherwise have been beyond physical capacity

TABLE IV—FREQUENCY WITH WHICH COLDS "WENT D TO THE CHEST" IN 300 CHRONIC BRONCHITICS AND CONTROLS

—	Bronchitic patients	Control
No colds	11	34
Colds do not go to chest	19	186
Colds do go to chest	270	80
Total	300	300

Blood-pressure

The mean blood pressures of the patients and did not differ significantly The mean systolic bl pressure of the patients was 148 4 mm Hg and of controls 142 8 mm Hg , the corresponding figures diastolic pressure were 88 3 and 84 1 mm Hg

If 160 mm Hg is regarded as the upper limit of no for systolic pressure and 90 mm Hg for diastolic, or other or both of these figures were exceeded by (27%) of the patients and 60 (20%) of the contr The difference between the proportions with hypertensi in the bronchitic and control groups is not significant

Clinical Features of 1000 Patients with Chronic Bronchitis

Age of Onset of Bronchitis

Table VI shows a clear pattern for the age of on of bronchitis First there are the catarrhal children do not throw off their respiratory infections In second decade fewer patients develop symptoms Af the age of 20 there is a rapid increase in the num developing bronchitis , the numbers remain st between about 30 and 60, and then decline

TABLE V—OCCUPATION BY MINISTER OF LABOUR'S CODE FOR 300 BRONCHITICS AND CONTROLS AGED 15–25

Occupational code	Bronchitic patients	Controls
I (Professional executive)	7	8
II (Intermediate)	11	9
III (Skilled clerical)	171	201
IV (Semi-skilled)	92	56
V (Unskilled)	12	9
Student	3	12
Housewife	3	3
Unemployed	1	2
Total	300	300

Mode of Onset of Bronchitis

The mode of onset of bronchitis was considered to be insidious in 524 and acute in 476. Patients having an insidious onset said that they gradually became 'chesty' over months and sometimes years. There was usually an initial period in which colds in the head were followed by expectoration which lasted a few days and caused no inconvenience. Sooner or later the bronchial infection was accompanied by a constitutional upset, after which the symptoms of infection or breathlessness persisted. Patients having an acute onset considered that the precipitating pulmonary infection was acute bronchitis in 342, pneumonia in 118, whooping-cough in 13, and measles in 3. Associated causes at the time of onset included coryza 140, influenza 72, gassing in the 1914–18 war 27, surgical operations 13, pleurisy 7, sinusitis 6, mental shock 6, and childbirth 3.

There is no sharp division between these two groups, but nearly all the patients felt that their symptoms had either developed gradually over many months or years or else had appeared suddenly after an acute respiratory infection. Indeed many in the acute group thought that a single respiratory infection suddenly converted them from healthy beings into respiratory invalids, and this was particularly so in the elderly.

Characters of Sputum ✓

Table VII shows the obvious increase in the *quantity* of sputum in the winter and during exacerbations of bronchitis. Some patients did not ordinarily expectorate at all; some stated that they swallowed any excess of bronchial secretions; others who would be regarded as having chronic bronchitis in a loose terminology perhaps would have been classified more correctly as having 'pure' emphysema.

TABLE VI—AGE OF ONSET OF BRONCHITIS IN 1000 PATIENTS WITH CHRONIC BRONCHITIS BY DECADES AND SEX

Age (yr.)	Males	Females	Total
0–9	74	37	111
10–19	50	16	66
20–29	128	41	169
30–39	157	33	190
40–49	169	32	201
50–59	194	19	213
60–69	44	2	46
70 or more	4	—	4
Total	820	180	1000

Inquiries into the *colour* of sputum were made in an attempt to differentiate between mucus and pus. The reliability of this method has been tested in another context and has been found to be accurate in more than 90% of cases. The figures demonstrate strikingly that in chronic bronchitis there is usually a mucoid sputum. Grey-white sputum was present in the majority both in summer and in winter; in about half of these it remained mucoid during exacerbations. A minority of patients, about a third, had mainly purulent sputum; 147 had purulent sputum all the year round and during exacerbations.

The *viscosity* of the sputum was described as loose and sticky with equal frequency.

The figures for the *time taken to clear the chest on waking* are included because of their very great importance to the patients concerned. No less than 367 patients indulged in that unpleasant ritual which causes at least a quarter of an hour's distress to themselves and to the other members of their households; in 222 the procedure extended into the summer months.

There was a history of *hæmoptysis* in 172 patients, 135 males and 37 females; it rarely amounted to more than blood-streaked sputum. This notoriously misleading symptom is very difficult to assess, and undoubtedly at times the blood came from sites other than the bronchi. Perhaps the safest plan is to accept the figure at its face value and to remember that, although chronic bronchitis is a recognised cause of hæmoptysis, there will always be some patients in whom the cause of a hæmoptysis is never discovered.

TABLE VII—CHARACTERS OF SPUTUM IN 1000 PATIENTS WITH CHRONIC BRONCHITIS

—		In summer	In winter	During exacerbations
Quantity	None	306	60	41
	Up to 1 oz.	351	328	96
	More than 1 oz.	343	612	863
Colour	Grey-white	547	669	350
	Yellow-green	147	271	609
Viscosity	Loose	367	470	—
	Sticky	327	470	—
Time taken to clear chest on waking	0–15 min.	428	448	—
	16–60 min.	222	367	—
	More than 1 hr.	44	125	—

Breathlessness

An attempt was made to differentiate between bronchospasm and constant breathlessness. Bronchospasm was regarded as a state of wheeziness in which the smaller air passages were apparently narrowed and unduly sensitive to changes in temperature, atmospheric impurities, and exacerbations of infection. Constant breathlessness meant abnormal breathlessness on exertion all the year round compared with healthy persons of the same age. Naturally many patients had both types of breathlessness.

Some 123 patients stated that they had no breathlessness; these were largely in the younger age-groups, being 25% of those aged less than 50 and only 6% of those aged 50 or more. Table VIII shows that 70·6% were considered to have bronchospasm and 52·1% constant breathlessness at the interview. No patient aged less than 20 was included in the series, and (see table VI) 346 patients stated that their bronchitis began at some time in the first three decades of life. Table VIII shows that 92 (26·6%) of these had proceeded to bronchospasm during these decades and 66 (19·1%) to constant breathlessness. These figures are far below the mean for the whole series and indicate that breathlessness is largely a symptom of middle or later life. Many of the

TABLE VIII—AGE OF ONSET OF BRONCHOSPASM AND OF CONSTANT BREATHLESSNESS IN 1000 PATIENTS WITH CHRONIC BRONCHITIS

Age-group (yr.)	Onset of bronchospasm	Onset of constant breathlessness
0–9	19	19
10–19	16	10
20–29	57	37
30–39	131	71
40–49	183	140
50–59	230	170
60–69	70	65
70 or more	4	9
None	291	479
Total	1000	1000

younger patients did not complain of breathlessness, their symptoms being largely attributable to infection

The differentiation between bronchospasm and constant breathlessness may seem to be unjustifiable and is defended on clinical grounds alone There is no doubt that the bronchi of most of the patients were abnormally sensitive to infections and changes in atmospheric conditions, and that a feeling of constriction was readily produced in such circumstances From the standpoint of treatment, especially prophylaxis, this symptom had to be carefully assessed By contrast, and often in addition, many patients seemed to have reached a state of constant breathlessness, presumably from a combination of mucosal œdema, chronic inflammation, bronchial secretions, and emphysema, but no attempt was made to assess how much of this could be attributed to emphysema

Clinical Assessment of Severity

A rough clinical assessment of disability was made in each case Some 341 patients were mildly disabled, having no more than occasional absences from work through bronchitis and being able to lead a normal life between attacks In the moderate group, numbering 435, respiratory symptoms were an appreciable handicap to ordinary existence, and often there were spells of sickness for several weeks or a few months The severely disabled, who amounted to 224 patients, could do no more than light work, and some were unfit to work at all

A relatively high proportion of the younger patients had a mild disability The moderately disabled were evenly distributed between the age groups The proportion of severely disabled rose from 13% of those aged less than 50 to 26% of those aged more than 50, reflecting the chronicity and progressive nature of the bronchitis and the diminution of respiratory reserve with advancing years

Ætiology

Reaction to Weather

The seasons of the year in which the patients considered their symptoms were worst were as follows winter 857, autumn 65, summer 37, and spring 24, the remaining 17 patients being unaffected by seasons

All the patients were specifically asked which atmospheric conditions adversely affected their bronchitis, affirmative answers being fog 744, wet 698, cold 435, hot 62, and dry 20 In addition, symptoms were aggravated in 440 on suddenly going from a hot to a cold atmosphere, and in 174 on going from cold to hot

Winter, being the time of unfavourable climatic conditions and also of respiratory infections, naturally sees an increase in exacerbations of bronchitis Fog was singled out as the most constantly aggravating climatic factor, but wet, particularly dampness as opposed to rain, was only slightly less frequently mentioned and probably accounts for the perpetuation of more bronchitis than fog because it is present so much more often in the London area The much lower incidence of aggravation by cold is significant Many patients who were considerably upset by fog and dampness firmly maintained that they were unaffected by dry cold, a feature which may have a considerable bearing on the choice of habitat and occupation

Smoking Habits

The numbers of non smokers were 40 (5%) males and 66 (37%) females The mean daily number of cigarettes among smokers was 18 5 for males and 11 8 for females, 1 oz of tobacco being equivalent to 30 cigarettes Table IX shows that more than half the smokers felt that smoking aggravated their bronchitis, and that a surprisingly large number had abandoned or reduced the habit with benefit

TABLE IX—TOBACCO HABITS OF 1000 BRONCHITICS

—	Yes	No	Don' kno
Does smoking aggravate bronchitis ?	479	381	3[illegible]
Has smoking been abandoned or cut down because of bronchitis ?	532	359	[illegible]
If " yes " has bronchitis improved ?	395	136	[illegible]

There were appreciably fewer non smokers among th 300 patients than among the controls, the figures 27 (9 0%) and 62 (20 7%) respectively The mean number of cigarettes among the smokers was simi in the two groups, being 18 2 for patients and 1 for controls

Home Conditions

Of the 1000 patients only 43 considered that hom conditions contributed to the onset of bronchitis, dampness was blamed by 22, other causes including air damage, overcrowding, and cold Home condition were considered to have adversely affected the course the bronchitis by 66 patients, 40 of whom blame dampness

Adverse Occupational Factors

Of the 1000 patients 177 were prevented from continuing in an occupation because of bronchitis, breathlessness was given as the main reason in 98, and exacerbations of infection in 67 Of the 177 thus prevented 114 found alternative work, most of the remainde were unfit to work or had retired, often prematurely, and only 4 were unable to find suitable work

The principal factors at work which the patient considered as aggravating their bronchitis were chang in temperature and draughts (175), dampness (148), co (132), dusts (129), smoke and fumes (111), and contracting infections from contacts (83)

There is no doubt that climatic factors exert a considerable influence on the symptoms of chronic bronchitis For those employed indoors the temperature and humidity of their place of work may well determine wheth they dare risk the journey from home Overc may lead to an excessive spread of respiratory infections Those who work both indoors and outdoors are particularly exposed to changes of temperature Outdo workers (many bronchitics prefer to work out of doors) are forced to regulate their activity to the prevailing climatic conditions, especially in the winter months.

Of the formidable array of dusts which were incriminated more than half were related to houses, coal, books and papers Others included wood shavings, packing materials, upholstery, paint, and flour Almost any seems to be a potential irritant Possible irritant specifically mentioned in this series—e g, asbesto cement, cork, wool, lead, lime, marble, printers' ink, talc and chromium—caused the patients to seek elsewhere

Fumes and smoke were another potent source bronchial irritation The products of combustion coal were mentioned most frequently Some 51 males aged 51–69, were exposed to gas in the 1914–18 war 27 of these dated the onset of their bronchitis to gassing and most of the remainder thought it aggravated th bronchitis, although sometimes the onset was man years after the gassing Among other irritants wer exhausts from motor cars, sulphuric acid, acetone benzene, caustic soda, and paint spraying

Discussion

Assessment of the clinical pattern of a slowly progressive disease like chronic bronchitis by the analysis of questionnaire can never be more than approximatel accurate However carefully the questions are framed the answers are bound to be influenced by personal bia on the part of both the patients and the interrogators These difficulties were overcome to a great extent in his series by the completion of a comparatively large number of forms and by limiting the interrogators to a few who knew each other well and worked in the same clinics The object of the investigation was to obtain information about the relative importance of some of the commoner clinical features of chronic bronchitis with a view to the study of selected aspects in greater detail at a later date

The high incidence of bronchitis among the relations of bronchitic patients, the figure being three times as great as for controls, suggests a hereditary predisposition This is probably the correct interpretation, since social and economic factors were eliminated as far as possible by making every effort short of visiting their homes o obtain comparable groups of patients and controls Also the part played by cross infection within the families although virtually indeterminable is unlikely to be important because of the late onset of bronchitis in most of the patients

Of the factors which aggravated the symptoms many were related to the quality of the inspired air Fog wet cold, and changes of temperature were frequent ources of irritation The habit of smoking tobacco had been curtailed or abandoned by more than half the patients. Various dusts fumes and smoke caused irritation at times Indeed almost any deviation from a clean warm dry atmosphere seems to be a possible source of aggravation of symptoms The effect of these features on the patients mode of life and capacity for work was often considerable.

Particular attention was paid to the characters of the sputum and the nature of the breathlessness since these comprise the outstanding symptoms of chronic bronchitis A review of the findings sheds some light upon the significance of infection bronchospasm and onstant breathlessness in this disease

Infection was considered to have been present at the onset of respiratory symptoms in every case It varied from a comparatively mild attack of bronchitis to a fulminating pneumonia At the time of interview 85% f all the patients stated that they had colds which went down to the chest, which strongly suggests the sustained influence of infection on the course of the bronchitis In 147 patients there was a purulent sputum in the summer and winter and during exacerbations These are the patients who can be labelled 'chronic bronchitis' with the greatest degree of confidence The part played by infection in the production of mucoid sputum is a matter of controversy Almost always the volume of sputum increased during exacerbations, and in about a third it remained grey white or mucoid Hence at least in some of these infection acted as a stimulus to the further production of mucus Whether or not infection alone can sustain a mucoid sputum through the winter months or all the year round is a uestion in urgent need of further clarification Of the 23 patients having no breathlessness, the majority had predominantly mucoid sputum which usually became purulent during exacerbations. To regard such patients having catarrhal bronchitis' is not entirely justifiable Certainly infection was closely connected with both the onset and the continuance of symptoms, but other factors—e.g., climate atmospheric impurities, and hereditary predisposition—undoubtedly played a part Indeed, here is the crux of the problem of the genesis chronic bronchitis Patients usually middle-aged men having been subjected to an intricate combination of environmental and hereditary factors for many years, find that pulmonary infection leaves them with an intractable mucoid sputum If this be designated a catarrh, an inflammatory basis is implied The alternative is to regard the infection as a sensitising agent which leads to overactivity of the mucus-secreting elements of the lungs Whichever is the correct explanation such patients are singularly prone to superadded bronchial infections.

No less than 70 6% of the patients were considered to have unduly sensitive bronchi and were regarded as being subject to *bronchospasm* In a way this figure is misleading because chronic bronchitis was not diagnosed unless there was a disability which persisted and at the time of interview 87 7% of all the patients had either spasmodic or constant breathlessness or both A large number of these patients, probably the great majority, would not have been regarded as having chronic bronchitis if they had not been breathless The relationship between bronchospasm and excessive mucoid secretions was not studied in this investigation but external stimuli particularly fogs seem to be incapable of producing one without the other

Constant breathlessness was present in 52 1% of the patients. Interpretation of the significance of this figure is not wholly possible. It is intended as a very rough guide to the incidence of emphysema Emphysema was not specifically investigated, and no physiological function tests were done The radiological findings showed good evidence of emphysema in 20% of the patients but this figure is undoubtedly an underestimate Emphysema is an almost invariable complication of chronic bronchitis, provided the bronchitis persists long enough but it is an insidious process and unless there is radiological evidence of bullæ, cannot be diagnosed in the early stages Hence bronchitics cannot be rigidly divided into those with and those without emphysema In a clinical sense, however advancing emphysema leads to increasing constant breathlessness, to which eventually cardiac insufficiency may contribute. If the present series is judged according to this symptom alone, there was suggestive evidence of emphysema in about half

Summary

A questionnaire was completed on 1000 patients with chronic bronchitis A comparison was made between 300 of these and 300 controls matched for age sex and social status

Chronic bronchitis is largely a disease of middle aged men

There is a fairly strong family history

The adverse effects of atmospheric conditions occupational factors, and smoking are discussed.

The types of sputum and breathlessness are considered

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REFERENCE

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I am feudal and a Taoist and use despotism with enlightenment for I am a doctor One has to impose upon the sick one's own will, and anything else is hypocrisy and nonsense Doctors use power so much and get so much pleasure out of it They stalk in their white gowns like prophetic kings; the stethoscopes round their necks are the badges of their magic knowledge they survey the prostrate forms of their patients, lying helpless in neat rows on their beds. They lay healing hands and save lives. This is arrant orgiastic power the most corrupting one to the soul that of doing good For it is so easy to believe that one is good —HAN SUYIN *A Many Splendoured Thing* London 1952 p 131

ORBITAL LEUCOTOMY

(ISOLATION OF THE ORBITAL CORTEX BY OPEN OPERATION)

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Early in the many published reports on the frontal lobe and its functions there have been references to a difference between its superior and inferior surfaces That there might be some such difference in function is not a very surprising possibility, but in the recent work on frontal ablations for mental disorder competent observers have come to the conclusion that the frontal areas are functionally equivalent

From a twelve years' clinical study of 300 cases of cerebral trauma Kleist (1934) concluded that there was a definite and recognisable difference between the syndromes resulting from lesions of the superior and the inferior surfaces of the frontal lobe involvement of the supero-lateral surface led to disturbances of intellect and psychomotor activity, whereas lesions of the orbital surface produced predominantly emotional changes, usually euphoria or simplicity, and less often depression with inactivity Though the precision of his conclusions has been criticised because of the type of material on which it was based, his work was a very thorough and painstaking attempt to differentiate the functions of the lobe on purely clinical grounds

Rylander (1939) also remarked that earlier workers had considered that the basal part of the frontal lobe played an important rôle in emotional life, and he believed this too, for in his own classical material he thought there were distinct changes in emotional tone in 22 out of 24 patients with lesions involving the orbital region

Experimental studies on the orbital cortex are mostly of recent origin, but Spencer (1894) found that faradic stimulation in the rabbit, cat, dog, and monkey led to respiratory arrest This and other autonomic changes have since been described by Bailey and Sweet (1940), Ruch and Shenkin (1943), and Delgado and Livingston (1948) Ablation of the orbital cortex in monkeys has been done in Fulton's laboratory by Livingston et al (1948b) the monkeys became active (but they gained weight in spite of this), easily tameable, and free from excessive fear In man Livingston et al (1948a) reported that stimulation of the orbital cortex transcortically during the exposure afforded by leucotomy also produced autonomic effects

McLardy and Meyer (1949), working on necropsy material have paid considerable attention to the differing effects of surgical lesions in various parts of the frontal lobe From an extensive study of clinical and anatomical relations they could find no great difference between the sites of lesions associated with clinical improvement and of lesions associated with the greatest personality change They suggested, however, that, from their evidence, there might be a rather greater association of clinical improvement with lesions involving isola- of the orbital cortex, but they emphasised that their result was derived from clinical material What is required is an alternat to the standard leucotomy which will produce co parable benefits without the undesirable side effe of the operation, principally personality changes a in some cases persistent incontinence and metabo disorders

Our trial of orbital leucotomy was based on the hyp thesis that the balance of evidence in the past has be that the orbital surface, rather than the superola surface of the lobe, is concerned with the predo emotional and affective aspects of behaviour, coupl with the working assumption that general personali damage is roughly proportional to the amount of front tissue destroyed In this sense we regarded the opera equivalent to a first step in narrowing down the full leuc tomy procedure In our final choice of the orbital we were influenced by the work of Scoville (1948, 194 who had introduced a technique for "undercutting"

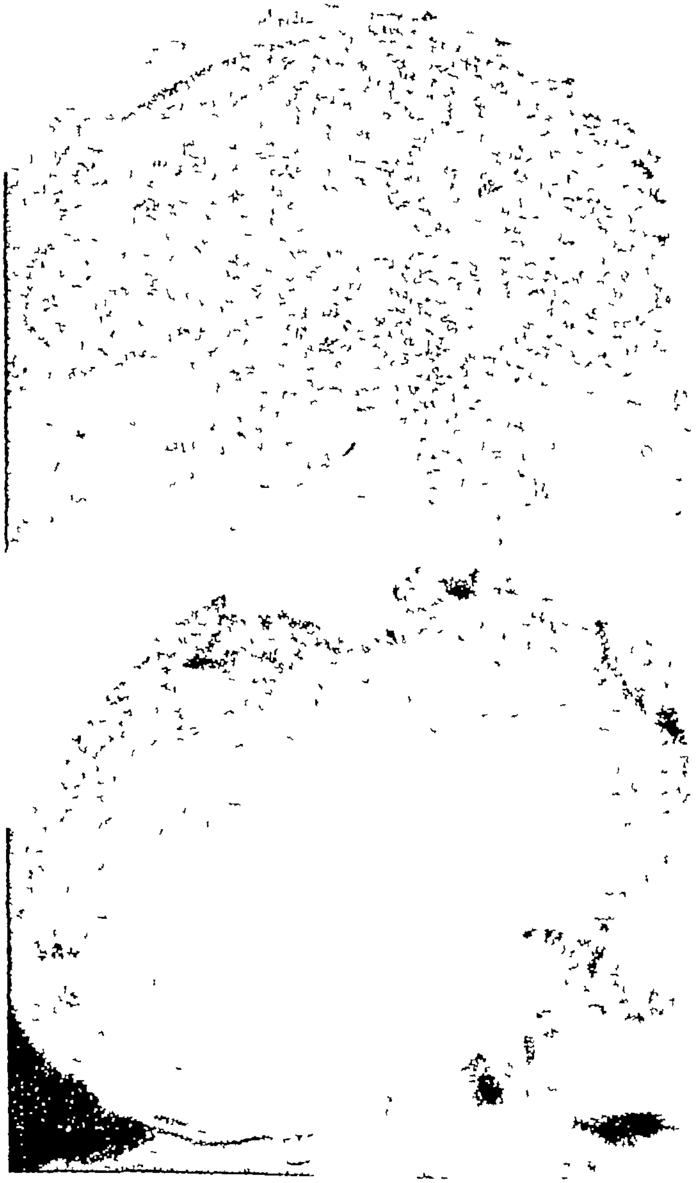

Fig 1—Radiographs of skull showing positions of trephine holes and silver clips site and depth of orbital leucotomy above, anteroposterior, below,

three surfaces of the frontal lobe. We were impressed by some of his early results from operating on the orbital cortex, and in this country some early trials of the operation by one of us with Mr Geoffrey Knight had yielded promising results. The operation follows closely Scoville's technique.

The Operation

The operation consists in making a line of cleavage with a brain spatula and a fine suction tube at the junction of the grey and white matter above the orbital grey matter on each side, extending from the frontal tips back to the level of the base of the anterior clinoid processes, with interruption of the long and short association fibres to the thalamus and to the adjacent frontal cortex. In some cases in this series it was found necessary to sacrifice a main venous tributary running across the face of the frontal pole, but apart from this no major vessels are divided. By operating under direct vision and with reference to the landmarks to be described below, one attempts to produce a discrete isolation of the orbital cortex without damaging, at least macroscopically, the adjacent frontal cortex or its blood supply. To confirm the site and depth of the section we have at the end of the operation placed silver clips mounted on small pieces of fibrin foam at the posteromedial limits of the section and taken postoperative radiographs. This method of localisation is open to the objection that the pieces of fibrin foam may not be placed accurately or may become displaced, particularly when cerebrospinal fluid is running freely. Nevertheless the position of the silver clips as seen in the lateral view (fig 1) gives some indication of the plane of section. Within these limitations the postoperative films in these patients confirmed that in 16 the operation had been limited to the orbital region. In the other 4 the clips were shown to be rather higher in the frontal lobes than usual, suggesting that in these instances more than the orbital cortex may have been isolated. Of these 4 patients 1 recovered, 2 were improved, and 1 was unchanged.

Technique

Preliminary radiographs of the skull are taken to determine the size and extent of the frontal sinuses. All our patients were operated on under general anæsthesia.

With the head slightly extended, a small coronal scalp flap is marked out at the anterior margin of the hair line. After the scalp has been incised, the pericranium and temporalis muscle on each side are cut in the same line and stripped down with the scalp to the level of the orbital ridges to expose the frontal bone subperiosteally. Bilateral trephine holes (3·75 cm. in diameter) are made lateral to the frontal sinuses, just above the orbital ridges and bounded by the lateral borders of the frontal bones (fig 1). On each side a cruciate incision is made in the dura to expose the anterior face of the frontal pole. A transverse incision, 2·5–3·0 cm. in length and situated 1·0 cm. above the orbital roof, is made in the cortex through to the white matter. The frontal pole is now lifted up as in a pituitary approach to the base of the anterior clinoid process. This represents the level of the posterior extremity of the cut to be made, and its distance from the cortical incision is measured. The direction of the orbital roof is also noted. Scoville's spatula forceps are inserted into the cortical incision parallel to the direction of the orbital roof, and, the blades being used as retractors, the white matter is sucked out with a fine sucker tip under direct vision. The medial limit of the posterior extent of the cut, over the clinoid region, is a good centimetre posterior to the lateral limit. Frequently when this point is reached, cerebrospinal fluid comes up from the cisterna chiasmatica. The medial and lateral borders of the section are defined by gentle suction until the grey matter on each side is reached. The depth of the section varies from 5·0 to 5·5 cm. (fig 2). Because the natural tendency is to angle the forceps upwards, direction and depth require repeated checking. *If the section is in the correct plane,* there is very little bleeding, and at the end of the operation it is not difficult to secure hæmostasis. The dura is closed with silk sutures, the bone discs are replaced, and the wound is sutured in layers.

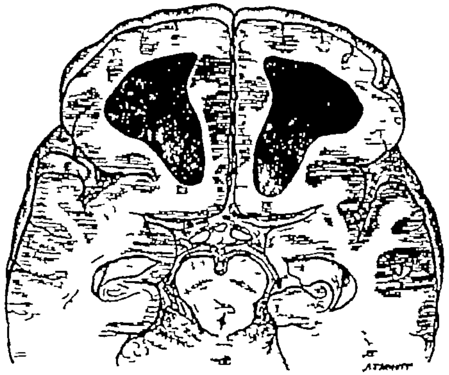

Fig 2—Brain preparation showing site of orbital leucotomy (black area).

Operative Risks

Between January, 1950, and December, 1951, 20 patients underwent orbital leucotomy [*]: they were aged 20–63, 4 of them being aged more than 55.

There were no operative deaths, and the only fatality in this series so far took place seventeen months after operation. This was in case 3, a female paranoid schizophrenic, aged 40, who improved sufficiently after operation to return home. She collapsed and died suddenly while alone in the house. Necropsy done elsewhere showed macroscopic evidence of cerebral atrophy and some pulmonary congestion; in particular no other intracranial complication was seen. Unfortunately, the brain was not made available for further study.

Recovery from the anæsthesia was uneventful: there was very little general disturbance, the wounds healed satisfactorily, and there was no postoperative infection or hæmatoma. In 1 case a clot was suspected three days after operation, but on re-opening none was found, and convalescence was satisfactory. The incidence of postoperative incontinence, epilepsy, and other changes is discussed below.

The Patients

All in this series were psychiatric patients in whom other treatments had failed to produce any substantial improvement in the mental state and, when surgery was considered, the possibility of spontaneous remission was remote. They all required hospital treatment: a typical state of affairs at the time of operation was that the patient had been ill for several years, usually becoming much worse, and that recently or within the preceding two years had become ill enough to need constant inpatient care.

The patients were aged 20–63: 11 being aged 20–40, 8 40–60, and 1 63. There were 9 men and 11 women. In all the clinical picture was florid, and the group was a fair sample of psychiatric inpatients. In half of them rapport was possible, insight was present in varying degree, and there was no extreme deterioration of the personality; in the others rapport was bad or impossible and degeneration of behaviour had begun.

Our patients were selected primarily by the presence of great tension and accompanying disturbances of behaviour: in fact our criteria were not very different from those now used by many physicians for standard leucotomy. However, from all patients referred for operation we selected for orbital leucotomy those who had exceptionally severe tension, anxiety, agitation, or outbursts of impulsiveness uncontrolled by other means In this series we did not include any very chronic or grossly demented schizophrenics The accompanying table lists the diagnoses

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[*] 1 other patient had a full orbital leucotomy during this period but after another psychosurgical procedure: therefore he has been excluded from this series.

10 of the patients were frank schizophrenics, of these 2 had exceptionally well preserved personalities, and 3 others were very well preserved for the type of illness involved By classical subgrouping, 1 was a schizophrenic simplex, 2 were catatonic, 3 were hebephrenic, and 3 were paranoid In the 10th patient the illness began in the puerperium She developed into a catatonic type of schizophrenic, there was no evidence of any infection All of these were disturbed patients, tense, suicidal, or impulsive 2 other patients exhibited schizophrenic features on occasions, but since they presented throughout their illness primarily as severe anxiety states, with constant tension and feelings of apprehension or dread, they have for brevity been referred to as such in the table

The remaining 8 patients had predominantly affective illnesses with depression 1 case of manic depressive illness presented mostly as mania

Results

The results have been assessed on the general clinical state of the patient compared with his preoperative condition, particularly as regards tension, impulsiveness, and aggression, features of particular interest in this series of patients The patients have been observed throughout their entire postoperative period to date, which now extends from one and a half to three years, all the discharged patients have been followed in their own homes Our experience is that recovery or improvement takes place in the first few weeks or months, and that its pattern does not differ significantly from that seen after standard leucotomy

RECOVERED (7 CASES)

7 patients have wholly and satisfactorily recovered from the illness with which they presented for operation They are all at home, and, although we are aware that this is not a universally valid criterion, in the case of 5 of them, who before operation seemed almost certain to be chronic hospital patients, this fact alone appears to be a good measure of their clinical recovery

In this group there were 5 patients (cases 4, 7, 14, 18, and 19) with essentially affective conditions All were able to be discharged symptom-free a few weeks after operation None has since had any relapse, and they have no complaints, on the contrary, 2 have repeatedly expressed their happiness and well being Case 4, called an aggressive psychopath, had at times had depression and also showed schizoid features, she had been in hospital for one and a half years Six months after operation she was discharged from hospital, and she has remained well since

Two other patients in this group (cases 6 and 12) were schizophrenic Case 6 was an unremitting catatonic type of schizophrenic and needed continuous care in a ward for disturbed refractory patients Her recovery took place gradually in the first three months after operation, and by the fourth month she was given full parole She was discharged, and six months after the operation she had completely recovered and was adequately caring for her house and family Case 12 was the only hebephrenic schizophrenic in the recovered group

The clinical details of 2 of these recovered patients are recorded

Case 7 —A married woman aged 39, first became ill twenty two years before operation When young she was normally sociable with a healthy range of interests She had her first attack of mania at the age of 17, and another four years later She would cease to sleep and would go off her food, soon she would be restless and confused talk rapidly and foolishly, and finally start doing acrobatics She saw men calling her to God Attacks gradually increased in frequency up to the end of her illness when she was rarely well for more than a week at a time She became more and more violent and in her attacks until these were regular features Occasiona the attacks of mania were preceded by a brief period depression and then at times she had been suicidal She been admitted to hospital on three previous Treatment by continuous narcosis had failed, and convulsive therapy, which had been given on several had been quite ineffective except in a most temporary

After operation she immediately became clear and oriented but was amnesic for the operation and for her episodes before it She was transferred to a quiet ward soon settled into a quiet orderly routine By three after operation she had several active interests, and months later she was discharged fully recovered Now, and a half years after operation, she has remained virtua symptom free to date—far longer than any recent remissi and is working happily and efficiently as a housekeeper

Case 12 —A woman, aged 35, first became ill some years before operation For two years her illness had consist only of generalised apathy, with bad headaches, loss appetite, and rather queer and unaccountable behav but she then began to develop bizarre thoughts and unpredictable behaviour, with much emotional disturba She complained to her doctor of awful dreams and of fears going mad She believed that everyone was trying to stop h from dying From then on she behaved in various erratic peculiar ways Often she seemed totally lost in hallu She said she had come from a grave, and asked people to c her throat She would look for a long time over her ri shoulder, and often she was silent for long periods Later she became totally inaccessible and manneristic, with stereoty repetitions She did not improve at all after twenty f electroconvulsive treatments, for a time she was given th treatments weekly because they seemed to help her slightly but it was eventually decided that a limited surgical operati would give her the best chance of a useful recovery

After operation —She was still very schizoid and fatuo in manner a month after operation, but could cc rationally if pressed Two months after operation she much less silly and fatuous and was a little euphoric She worked well in the hospital laundry and continued to

CASES AND RESULTS

Case no	Diagnosis	Duration of illness before operation (yr)	Length of follow up after operation (yr)	Result
1	Chronic anxiety state	14	3	Improved slightly
2	Paranoid schizophrenia	12	3	Improved 2 month relapsed
3	Paranoid schizophrenia	9	$1^{1}/_{2}$	Improved (died later)
4	Aggressive psychopath	11	$2^{3}/_{4}$	Recovered
5	Manic depressive psychosis	4	$2^{3}/_{4}$	Improved
6	Schizophrenia catatonic	2	$2^{3}/_{4}$	Recovered
7	Manic depressive psychosis	22	$2^{3}/_{4}$	Recovered
8	Paranoid schizophrenia	8	$2^{3}/_{4}$	Improved 6 m relapsed
9	Involutional melancholia	11	$2^{1}/_{2}$	Improved
10	Agitated depression	5	$2^{1}/_{2}$	Improved
11	Hebephrenic schizophrenia	2	$2^{1}/_{2}$	Improved 9 month relapsed
12	Hebephrenic schizophrenia	7	$2^{1}/_{4}$	Recovered
13	Catatonic schizophrenia	3	2	Improved
14	Agitated depression	3	2	Recovered
15	Schizophrenia simplex	6	2	Improved
16	Agitated depression	10	$1^{3}/_{4}$	Improved 2 month relapsed
17	Hebephrenic schizophrenia	13	$1^{1}/_{2}$	Improved slightly
18	Chronic anxiety state	4	$1^{1}/_{2}$	Recovered
19	Agitated depression	12	$1^{1}/_{2}$	Recovered
20	Catatonic schizophrenia	6	$1^{1}/_{2}$	Unchanged

7 recovered 8 improved 5 no change

in a placid way Nine months after operation she was discharged recovered and obtained a simple repetitive part-time job Three months after this she was offered a full time job in the same firm, and she has remained well and self supporting to date two years after operation

IMPROVED (8 CASES)

In this category have been placed those patients who after operation have been freed from any of the dominating or persisting symptoms of their presenting illness have gained contact with reality or have achieved a generally more useful adaptation

The improved group includes 4 schizophrenics who had been ill for three six, nine and thirteen years and were subject to severe outbursts of violence and aggression There has been no return of these outbursts since operation The other 4 rated as improved had affective disorders in which there was constant tension and much subjective suffering which disappeared at various lengths of time after operation In 1 case of chronic anxiety state there has recently tended to be some slight return of tension but with this exception these patients have remained quite free from objective signs of tension and subjective feelings of anxiety

4 of these patients have been discharged from hospital of these 2 are now working two and a half and two years after operation, and a 3rd was coping adequately with all her housework until the time of her sudden death seventeen months after operation. The other 4 patients are still in hospital but are more generally sociable and active With the major symptoms of their illness removed they enjoy a happier and much less disturbed existence Case 9 illustrates the type of improvement seen in this group

Case 9—A single woman aged 60 had worked for one employer for thirty years She was always healthy until the outbreak of war In 1939 with the menopause she became depressed and developed ideas of reference of various kinds She heard voices giving her religious instructions. She thought her doctor was trying to influence her thoughts, and felt guilty of being unable to catch their religious significance Early in 1940 she left her employer suddenly and without warning and gave herself up to the police She declared that she was responsible for the war She was admitted to hospital under certificate and remained depressed and hallucinated for a year but after a second year she left the hospital Four years later she again had to be certified. Now she was actively hallucinated and had made various suicidal attempts saying that she preferred to die than to lead a wicked life She had a large amount of convulsion therapy with both leptazol and electricity but after four more years in hospital she remained just as hallucinated *profoundly depressed*, and actively suicidal. Her personality remained reasonably well preserved

After operation she seemed rather quiet and a little less depressed, and could be made cheerful and to smile more easily She said she felt happier She remained subdued but was no longer hallucinated or suicidal She continued to improve took an active interest in simple affairs about her and went out on visits frequently Clinically she is greatly improved but because of her age and friendlessness and the difficulty of getting her somewhere to go she has been unable to leave hospital.

Case 3 is also recorded for until the time of her sudden death, seventeen months after operation, she had exhibited a fairly typical pattern of improvement.

Case 3—A married woman, aged 40 had been a paranoid schizophrenic for nine years at the time of operation She had been hostile towards her husband and adopted son and was eventually certified because she was a danger to her husband who was an invalid. She was generally arrogant irresponsible querulous, and noisy; often she was negativistic. Sometimes she became violently hostile and aggressive She later became rambling and incoherent in her accounts of her persecution, and eventually talked of nothing else but her son's wrongdoings. She was quite without insight.

After operation she very soon became quieter and was composed and sensible The framework of delusions about her adopted son was still elicited on questioning but she no longer mentioned it spontaneously and this in her case represented a great change She would even inquire about him in a kindly way and no hostility was evident. Her husband was delighted ' with her During the next six months she continued to improve and became coöperative sociable and a very willing worker She was euphoric for a time and was then garrulous, without foresight and content to live for the moment After operation her delusions never again had any emotional force She needed no more sedative drugs She was discharged at six months and continued happily until her sudden death

UNCHANGED (5 CASES)

Of these 5 patients 4 (cases 2 8 11 and 20) had been schizophrenic for twelve eight two and four years and the 5th (case 16) had had severe agitation and depression for ten years They now show little change compared with their preoperative state However it should be noted that 4 of them made considerable temporary improvement after operation and for a much longer time than after any previous treatment but all relapsed three within two months of the operation, and 1 (see below) nine months after operation. 1 schizophrenic (case 8) is *still free from the violent behaviour and impulsiveness* exhibited preoperatively but his condition is otherwise unimproved and he cannot be regarded as having made any substantial gain

Case 11—A man aged 22 was discharged on psychiatric grounds from the R A F He had behaved oddly talked to himself and been very strange and solitary Later he became aggressive and resentful fought his adoptive father and smashed windows. He developed into a very noisy hallucinated schizophrenic abusive and threatening Often he was extremely aggressive and would mutter to himself and roll on the floor Some of the time his manner was euphoric and happy go lucky He had a long course of insulin but never went into coma, though he reached a dose of 270 units. He improved physically but not mentally He had also a course of electroconvulsive therapy and another of continuous narcosis with paraldehyde and hyoscine A preoperative electro encephalogram was abnormal suggesting a constitutional dysrhythmia with a psychomotor variant A pneumo-encephalogram was within normal limits

After operation he immediately became quieter rational and coöperative For a short time he was even lethargic. He was never incontinent, but he had an epileptic fit at one week and another at four months after operation. After a few weeks he had a few minor outbursts, but not approaching the preoperative ones in force In general he improved mentally and became well enough for discharge The improvement however only lasted until nine months after operation, when after an episode of window smashing he was readmitted and is now essentially the same as before operation.

Effect on Personality

In our experience to date this operation has proved relatively free from undesirable psychological complications. Sometimes there is undue apathy or lack of initiative sometimes slowness with apparent lack of energy sometimes facility or fatuity once we observed severe but temporary disinhibition of an unpleasant character—all changes seen after leucotomy but never so pronounced Standard intelligence tests do not reveal any *significant change in intellectual ability* We can thus fully agree with the experience of Scoville et al (1952) that the operation does not cause serious intellectual or temperamental damage and is to be ' recommended because of its nearly complete preservation of the personality

Rylander (1952) also discussing operations which involve isolation of the inferior surface of the lobe, has stated that in his experience undesirable personality changes are always minimal personality change which does occur is of the same type as after standard leucotomy but not so pronounced

Unwanted personality changes are common after standard leucotomy the actual incidence one attributes to this operation depends on the criteria one adopts but in a small number probably about 10% there are serious symptoms and disturbances of behaviour which give rise to most unpleasant and incapacitating post operative syndromes At the other extreme, after very small lesions, changes of this magnitude are never seen Scoville and his associates attribute this absence of all serious deficits after the orbital operation to the purely quantitative fact that only about a third of the frontal-lobe connections are interrupted Briefly, we have in our personal experience, for such a quantitative comparison, two other similarly studied series one of full standard leucotomy (Tow 1952), and one of anterior cingulectomy (Tow and Whitty 1953) in which less than 4 c cm of cortex suffers interference on each side The personality changes which we have observed after orbital leucotomy approximate in quantity to those in anterior cingulectomy, though they differ in quality We have consequently been impressed with the smallness of any personality deficiencies in this series compared with those resulting from the standard operation If there is a typical postoperative personality picture it is that of a generally quiet, placid, and—in the extreme—even timid personality with a possible slight blunting of comprehension or mental acuity Gross postoperative abnormalities in behaviour have not been seen

Other Changes

Behaviour —Before operation these patients almost all showed some kind of disturbed behaviour 11 were subject to the most violent and uncontrollable outbursts , and 8 others were either violent and aggressive at times or a great suicidal risk The effect of operation has been extremely satisfactory In over half the patients the disturbance of behaviour disappeared immediately after operation and has not returned , in the others the improvement was neither immediate nor dramatic, but behaviour was favourably affected in all

Sleep —In general this has improved 7 patients have shown very considerable improvement , 3 of these sleep well without aid, whereas before they regularly needed hypnotics

Weight —10 patients gained in weight, but some have now begun to lose weight again, and the residual gain at present is mostly only a few pounds 1 has gained 4 stone, and 2 more 2 stone each

Sedatives —Several of the patients need fewer drugs, such as hyoscine, 'Amytal,' and paraldehyde There has been some fluctuation, both before and after operation, in the need for heavy sedation, but at least half the patients need considerably less than preoperatively

Complications

Epilepsy —Of the 20 patients 2 have had epileptic fits after operation, but in neither have the attacks been frequent In 1 case the first fit took place eight weeks after operation, and over the next three years there were two further attacks at six months and nine months In the other case the patient showed a dysrhythmia suggesting epilepsy on the preoperative electro encephalogram , his first fit occurred a week after operation, and he had one more attack over the next two and a half years, at four months after operation So far, with the average follow up of two years, no patient has begun to have epileptic attacks for the first time after the early postoperative period The patients were not given prophylactic anticonvulsant therapy Electro encephalograms were made preoperatively and from one and a half to three years later in 15 of these patients, and no significant changes were seen

Incontinence has been minimal compared with its incidence after standard leucotomy 1 patient was regularly incontinent of urine for the first two weeks and was once incontinent of fæces , a 2nd patient was incontinent for five days , and 3 others had occasional incontinence during the first postoperative month , but in all the cases full control was re-established

Discussion

A large body of conservative psychiatric opinion accepts leucotomy as an available routine treatme Many feel that it is illogical but that circumstances for them to use it in certain cases in which experience h now shown that it yields an improvement otherw unobtainable The fact, however, that it may have some advantages over other empirical methods no reason why one should accept its disadvant unperturbed If in the absence of what may be rational methods—for appropriate cases—cerebral su gery is proving to be a valuable therapeutic approach, becomes more, rather than less, important to seek ope tions which do the greatest good and the least bad

With the current interest in this problem there ha come to be two distinct opinions one that the tot clinical change produced is proportionate simply to amount of cerebral tissue destroyed , and the the change is in some way related to the particular involved Evidence has accumulated on both The work of Meyer and McLardy has now yiel many valuable correlations , but there is still no clinical guide to what exactly should be cut in indi clinical syndromes There is, in fact, still no dec evidence about the relative merits and demerits of different incisions In practice there has developed an attitude of caution towards the major operation but with great uncertainty about what to use in its place The suggestion of Sargant and Slater (1948) is that where it is possible to conduct the operation in stages it is best to start anteriorly, a second and more posterior cut being possible if the first does not produce the desired effect Thinking on these lines, however, we suggest that it may be more informative to make the first incision in definitely selected part of the frontal lobe (so far as surgically possible) A suitable part is the whole of o surface We agree with the implication of Sargant Slater that, as a routine substitute for the major tion, it is not yet practicable to use anatomical v of very precise location However, an incision a the whole of one surface, and a standard leucotomy, more likely to result in two unequivocally discrete than is an attempt first to produce an anterior image the standard cut , and so in the long run such a may be more useful and informative

On balance, the effect of orbital leucotomy seems t be at least as good as that of standard leucotomy bu with fewer undesirable complications The results in typical but small group of cases compare well with clinical results after the standard operation There ha been no death due to the operation in this series, and th results so far indicate that there is far less likelihood any permanent physical complication or of any seri damage to the personality Although the patients in series were not all of the worst prognosis, the results very considerably better than could be expected other forms of treatment The numbers involved small, but half the patients with affective disorders recovered after illnesses with an average duration of te years The effect on violent behaviour has been extrem satisfactory Half the schizophrenics have improved, only a sixth have recovered The important however, is that whatever recovery has been obtaine takes place in the first few weeks or months , provided such a recovery lasts, this possibility, procuring early relief in an illness likely to last for year must always be an argument for the use of surger

The results in this series so far suggest that orbit leucotomy produces therapeutic results comparable those of prefrontal leucotomy but with much less person ality damage, and it seems to be worthy of further tri in some cases where relatively major surgery is thoug necessary for the treatment of mental illness In impu and violently disturbed active psychotics and in chron affective disorders with great tension and anxiety it may be the operation of first choice after all non surgical treatments have failed

Summary

The operation of orbital leucotomy is described It is an open operation and consists of a horizontal incision in the white matter just above the orbital cortex

Of 20 patients with various psychiatric disorders operated on two years ago 7 have recovered and 8 more have improved.

There was no death due to the operation

Because physical and psychological complications are minimal and beneficial effects are comparable with those of prefrontal leucotomy orbital leucotomy is recommended for trial particularly in patients with severe intractable tension and disturbed behaviour, as a common alternative to the standard operation

These patients were referred to us by Dr R W Armstrong, Dr John Duffield and Dr William Ogdon who have throughout the work helped in the assessment of results We thank Miss F M Taylor for performing the electro-encephalography; and Miss A. Arnott for the illustration. We are grateful to Dr R G McInnes and Dr Ian Skottowe for helpful criticism

This work was done under the direction of the late Sir Hugh Cairns, who performed all the early operations

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PYREXIA IN THE PUERPERIUM

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IN 1950 it was decided to investigate the present causes of pyrexia in the puerperium Clinical observation had suggested that the present-day practice of obstetrics had altered the type and site of infections responsible for a rise of temperature in the puerperium from those commonly described in the textbooks In addition changing conditions had led to some inaccuracies in the returns made of notifiable pyrexia and a false over all picture was being obtained The unsatisfactory position regarding notification has been clearly stated by Gordon (1951)

It was also felt that a careful analysis of all the cases of pyrexia in the puerperium during a definite period might provide a basis for the revision of the existing standard of notifiable pyrexia. During the period of the investigation however the regulations for notification of puerperal pyrexia were altered by the Ministry of Health and the present standard of a temperature of 100·4° F occurring once in the fourteen days after delivery was adopted How far the new standard is an improvement on the old and what might constitute a satisfactory alternative method of notification are discussed below

In any consideration of puerperal pyrexia it is helpful to understand how the present position of notification and the emphasis on uterine infection have arisen

Mayrhofer (1865) showed that the streptococcus was the probable cause of puerperal fever and Pasteur (1879) established beyond doubt the connection between this organism and death from puerperal sepsis The streptococcus continued to dominate the obstetric scene and notification of puerperal pyrexia was introduced in an attempt to check the spread of this infection

In 1932 Colebrook with his colleagues attacked the problem of streptococcal infection in midwifery and in the ensuing years published a series of papers emphasising the necessity for the control of throat carriers and the importance of detailed antiseptic technique in reducing the incidence of infection It was not until the classic paper of Lancefield and Hare (1935) that the significance of the group A streptococcus became apparent. The connection with erysipelas, scarlet fever and streptococcal tonsillitis became obvious, and the confusion caused by the presence in the vagina of relatively non pathogenic but hæmolytic streptococci of other groups was clarified

The use of 'Prontosil' in streptococcal infection was described by Domagk (1935) and its use in obstetrics was investigated by Colebrook in 1936 Since Colebrook and Kenny (1936) reported the successful treatment of streptococcal uterine infection the organism has lost much of its terror and with the discovery of penicillin sepsis has become a very rare cause of maternal death in this country

Arguments about pyrexia in the puerperium have waged since the days of White and Gordon in the late 18th century and there are many papers discussing the causes of pyrexia, notable contributions being those of Lea (1910), Little (1905) and Stander (1945) Two major points arise from the study of the historical background to this subject (1) emphasis was always on mortality and not morbidity and (2) organisms are mentioned which are not now regarded as normally pathogenic Relatively little attention was paid to the extragenital infections, and there is a dearth of new information available from the period following the work of Colebrook and his colleagues

It is well known that sepsis is virtually never a cause of maternal death at present in fact there has been only one such case (due to *Clostridium welchii*) in the last six years at this hospital, during which time some 15 000 patients have been delivered Nevertheless puerperal pyrexia remains a common cause of maternal morbidity and may lead to a longer stay in hospital In all that follows the difference between puerperal sepsis and puerperal pyrexia is important Confusion between these two still exists despite the fact that every book or paper emphasises the distinction It is puerperal pyrexia—a rise of temperature in the puerperium—with which we are dealing Puerperal sepsis or infection of the genital tract with pathogenic organisms will be seen from what follows to be much more uncommon

Investigation

All patients who in 1951 had a raised temperature were submitted to a full clinical examination and a high vaginal swab and a catheter specimen of urine were examined. This routine was practised whenever the temperature rose above 99·4°F on any occasion.

Bacteriological Methods

The methods by which these specimens were examined were as follows

On arrival in the laboratory the high vaginal swab was inoculated on two blood-agar plates and a direct film was stained by Gram's method. One blood-agar plate was incu bated aerobically, and the other anaerobically, for eighteen hours or, if necessary, forty eight hours, and the plates were then examined by standard methods (Gibson and Calman 1953) Organisms were picked off for special investigation when required, and provisional reports were issued at once The direct film was examined, and the amount of pus present was reported in addition to the presence of organisms

A sample from the cathether specimen of urine was centrifuged and its deposit examined, both a wet preparation and a gram stained film being used The spun deposit was cultured aerobically on blood agar and MacConkey's agar

Steps in Investigation

Every effort was made to give some guidance to the clinicians twenty-four hours after receipt of the specimens, so that isolation and other measures could be applied without delay, treatment was not delayed for bacteriological tests if it was thought to be urgent

The investigation fell into three parts (1) the whole of the group was reviewed, (2) an attempt was made to correlate these pyrexias with obstetrical manœuvres or other occurrences which are supposed to cause pyrexia, and (3) only those cases were considered in which a notifiable temperature of 100 4° F was reached

So that no case should be missed, all the notes were examined by the records officer, who selected all those in which a temperature of 99°F had been charted, all patients who had a known rise in temperature in the twenty four hours before delivery being excluded from the survey This produced the large number of 1423 cases out of 2701 patients delivered in 1951 All these were next checked against the laboratory records to trace any reports which had been incorrectly filed The whole group were then examined in detail, and 469 were rejected because they had not reached the standard of 99 4°F This left 954 cases in which the temperature had been above this figure, each case being scrutinised and an attempt being made to group them as either purely obstetrical or medical conditions occurring without particular relation to the pregnancy, the bacteriological reports being used to check the clinical findings

General Findings

The 954 cases were divided into the following groups

	No of cases
Pyrexia of no significance	499
Genital tract	141
Urinary	132
Breast	48
Non-obstetric	71
No cause found	63

The 499 cases of pyrexia of no significance consisted mainly of patients whose pyrexia, often in the day following delivery, was slight and not maintained In these cases also the pyrexia settled within twenty-four hours without treatment, symptoms, or positive findings In contradistinction the 63 cases in which no cause was found consisted of patients who had a definite and continued pyrexia, but in whom clinical and bacteriological investigation yielded no result This group also contained those cases in which bacteriological examination was inadvertently omitted

Other difficulties arose in classifying these cases

(1) The same pathogen was sometimes isolated from both high vaginal swab and catheter specimen of urine In these cases the presence of a considerable number of pus cells in either site was taken as the deciding factor

(2) In some cases the temperature was high but the bacteriological and clinical findings were not substantially significant To avoid classifying such cases on inadequate grounds they were labelled "no cause found"

(3) In some patients a pathogenic organism was isolated but with a minimal rise of temperature, these were reluctantly placed in the relevant group

Genital tract Infections

The decision to include cases in this category was made on an assessment of clinical and bacteriological findings taken together The presence of clinical signs, of known pathoge organisms, and of intracellular organisms in the purul discharge, and the response to treatment were all us to decide whether a case should be placed in this cat or not For instance, the one case in which *Staphyl coccus albus* is listed as the causal organism was d on definite clinical evidence and response to treatment

The organisms isolated from the high vaginal swa in the 141 cases of genital-tract infection were follows

Organism	*No of*
Anaerobic streptococcus	48 (34 0%)
Aerobic non hæmolytic streptococcus	19 (13 5%)
Staph albus	1 (<1·0%)
Bact coli	8 (6 0%)
Strep viridans	11 (8 0%)
Diphtheroids	1 (<1·0%)
Diphtheroids and *Bact coli*	2 (1 5%)
Diphtheroids and *Staph albus*	3 (2 0%)
Staph aureus	23 (16·4%)
Cl. welchii	1 (<1·0%)
β hæmolytic streptococcus group C	1 (<1 0%)
β hæmolytic streptococcus group D	2 (1 5%)
β hæmolytic streptococcus group G	8 (6 0%)
β hæmolytic streptococcus (ungroupable)	8 (6 0%)
Gonococcus	1 (<1 0%)
Strep viridans and *Bact coli*	1 (<1 0%)
Anaerobic streptococcus and *Staph. aureus*	1 (<1·0%)
No significant organism isolated	2 (1 5%)
Total	141

The distribution of organisms differs from that reported by other workers (Little 1905, Stander 1945) Th notable feature is the complete absence of group A hæmolytic streptococci, recently, however, an outbreak of infection due to this organism occurred in this hospit (Gibson and Calman 1953) The importance of anaerob streptococci is clear, and *Staph aureus* seems to be frequent pathogen, this later organism appears to b responsible for more infections than previously occurs often in various types of infection throughout th hospital Many of the other organisms reported may fact be saprophytic and not related to infection

Urinary tract Infections

The organisms isolated from 132 cases of urinar tract infection were as follows

Bact coli	96
Strep fæcalis	11
Mixed growth	18
Staph aureus	5
Paracolon	2

In assessing such cases more importance was placed on th presence or absence of pus than on isolation of th organism alone, and in all these cases pus cells wer present in fair numbers

The organisms isolated from the urine show th expected preponderance of coliforms The place of the fæcal streptococcus as an infecting organism in th urine is not entirely clear, because the urine can easil be contaminated with this organism while the is being collected Nevertheless in some cases strept cocci are seen alone together with pus cells and m be regarded as causing the infection On the other hand the occasional case in which *Staph aureus* was isolat is in keeping with the frequency with which the organis is being found in other sites

Breast Abscess

The criteria for accepting the breasts as a cause o pyrexia were strict, engorgement alone being accepte in only 2 cases out of 48, in both of these there were n other positive findings and the temperature sett without treatment at the same time as the engorge ment subsided In 13 cases pus was obtained eith by incision or by expression *Staph aureus* being causal organism in each case In the remaining 3 cases the mastitis was definite and subsided with anti biotic treatment

Non-obstetric Causes

In this group were placed such things as minor seps excluding that of the genital tract, and general medic conditions, they were as follows

	No of cases
Thrombosis and hæmatoma	19
Chest	23
Upper respiratory tract	24
Minor sepsis	3
Enteritis	2
Total	71

Of the patients with infections of the chest and respiratory tract 14 had undergone general anæsthesia this represents only 0·5% of the patients anæsthetised during the year

No Cause Found

There remained a substantial group of 63 cases (14%) in which we were unable to discover any cause for the rise in temperature

Correlation of Pyrexia with Previous Events

The second part of this investigation was an attempt to correlate the pyrexia with any predisposing cause such as obstetric manœuvres and blood loss

Infections of Genital Tract

92 cases (65%) had experienced some interference or tissue damage the manœuvres performed in these cases were as follows

	No. of cases
Episiotomy	42
Tears	36
Manual removal	5
Cæsarean section	9

This left 49 cases (35%) in which delivery was spontaneous without tears or interference We were unable *to show any clear relationship to delivery by forceps* the 77 cases in which there were tears and episiotomies containing almost equal numbers of spontaneous and forceps deliveries (In 95% of all forceps deliveries an episiotomy was done)

Manual Removal

This was done on 52 occasions in the year 8 of these patients had a rise in temperature 2 being due to urinary infections in the remaining 6 the genital tract appeared to be the site of infection, the infecting organisms being *Cl welchii* anaerobic streptococcus, *Bact coli* (2 cases) *Staph albus* and *Strep viridans*

Cæsarean Section

After 39 of the 117 such operations there was a rise in temperature to 99·4°F the causes of the pyrexia being as follows :

	No. of cases
Genital infection	9
Urinary	8
Thrombosis and hæmatoma	3
Medical	1
Temp. 1st 24 hours only	9
No cause found	9

Blood-loss

During the year under consideration 111 cases of postpartum hæmorrhage occurred, and of these 35 reached the 99 4°F level of pyrexia ; in addition 4 other patients with this pyrexia had an antepartum hæmorrhage *These figures showed no greater incidence* of pyrexia than the number that would be expected in 111 deliveries since about a third of all the patients delivered during the year reached this standard of pyrexia (see above) We were therefore unable to show any close relationship between blood loss and pyrexia

Comments

In the same way we attempted to relate infections of the urinary tract to obstetric manœuvres but the results were inconclusive, except as regards cæsarean section in which group 20% of the pyrexias were due to infections of the urinary tract.

The rôle of trauma in predisposing to infection has not been established in our cases, but this may have been influenced by the fact that all the patients were treated in hospital and that usually we did not have any severe infections within this period Whether the effect of trauma on the infection rate would have been greater if treatment of shock and hæmorrhage had been less adequate is an open question

In considering the bacteriology of genital tract infection it was remarked that many of the organisms might be saprophytic We felt that in many instances organisms were isolated from the high vaginal swab which can be shown to be present in the vagina of normal patients and cannot be *regarded as always pathogenic* when isolated from a patient with pyrexia In some cases however organisms of low virulence can cause infection in damaged tissue

This has led us to investigate afresh the whole question of uterine and high vaginal swabs as a method of diagnosis Previous work on the interchangeability of these methods has largely been related to infections with the hæmolytic streptococcus, and with the changes in emphasis which we have found the situation has altered considerably The results of the further investigation although incomplete throw considerable doubt on the value of the high vaginal swab in non-streptococcal cases of pyrexia

It does seem however, that the cases which have clinical signs of uterine infection are also those in which the bacteriological findings are unequivocal ; and, *further that many cases considered to have low grade* uterine infection on the results of high vaginal swab examination do not in fact have more than local trauma and absorption of autolysed tissue as a cause of their pyrexia

Notifiable Pyrexia

The third part of our investigation concerned those cases in which the new Ministry of Health standard of 100 4°F was reached. This occurred in 188 cases (7% of the year s total) as follows

	No of cases
Urinary tract	55 (29%)
Genital tract	49 (26%)
Non-obstetric	30 (16%)
Breast	21 (11%)
No cause	33 (17%)

It is interesting to compare this distribution with Gibberd s (1947) classification of 378 cases of notifiable pyrexia at Guy s Hospital in 1928–37

Total number of cases	*188*	*378*
Genital	26%	54%
Urinary	29%	18%
Breast	11%	7%
Respiratory and other infections	16%	21%
No cause	17%	—

There are two obvious major differences in the present series : (1) the decrease in genital infection and the corresponding relative increase in urinary infection ; and (2) the presence of a ' no cause found ' category This classification is necessary because of two factors (*a*) pyrexia occurring once only requiring notification, and (*b*) pyrexia within twenty four hours of delivery being notifiable In the past few years the rate of notifiable pyrexia (according to the old standard) in this hospital and other similar units has stood at about 3% judged by the published reports The notification rate will be at least doubled by the new standard the publication of figures resulting from the increased rate of notification may produce unreliable or even alarming appearances Of the 188 cases of notifiable pyrexia listed above only 26% were due to infections of the genital tract and of them more than half were clinically mild , hence perhaps 10% of all notifiable cases (18 cases in the year) had a moderate or severe genital infection As regards cæsarean section 22 cases out of 117 (19%) reached the new notifiable temperature in 8 of these cases the pyrexia occurred only in the twenty four hours after operation and in 2 others the pyrexia occurred once only without positive findings Therefore in 10 out of 22 notifiable cases the temperature settled without treatment or positive findings. (Of the remaining 12 patients only 3 appeared seriously ill.)

Conclusion

We feel that, if an alternative can be devised which would involve notification of cases of true genital-tract infection only, this would encourage notification of exactly those cases for which this procedure was devised The main object of notification is to bring infectious diseases under rapid control and to prevent their spread from patient to patient the only important cause of puerperal pyrexia which falls within the scope of this objective is infection of the uterus by hæmolytic streptococci belonging to Lancefield's group A We therefore suggest that the older practice of notifying cases of uterine infection rather than puerperal pyrexia should be restored Today general practitioners are accustomed to cooperate with the Public Health Laboratory Service in the control of infectious diseases—e g, diphtheria—and it might be that confining notification to proved streptococcal cases would give more evidence of epidemiologic d value than does the present system

If, on the other hand, this is felt to be impracticable, we think that notification as a whole should be abandoned We do not consider that further adjustments in the level of pyrexia would serve any useful purpose

Summary

All cases in which there was a rise of temperature in the puerperium during 1951 at Queen Charlotte's Hospital are reviewed and classified according to cause and relationship to obstetric manœuvres

The incidence of notifiable pyrexia is discussed and the present standard considered

We wish to thank Dr John Murray and Mr G F Gibberd for valuable advice, and the staff of the records department, especially Miss Jacobson, the records officer, for the initial separation of the pyrexial cases

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CERVICAL SPONDYLOSIS SIMULATING MOTOR-NEURONE DISEASE

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THE neurological manifestations of cervical spondylosis are described in detail by Brain et al (1952) in a comprehensive article in which they report medical and surgical experience with 45 patients of their own These workers draw attention to the extraordinary variations in the mode of presentation of the disorder

In a large proportion of cases of cervical spondylosis sensory symptoms and signs differentiate the disorder clearly from any form of motor-neurone disease That confusion can arise, however is shown by Brain's allusion to cases in which amyotrophic lateral sclerosis had previously been diagnosed. Failure of the condition to progress led to subsequent review of these patients, and they were found to have cervical spondylosis.

We have recently become aware that cervical spondylosis may also produce a syndrome closely resembling progressive muscular atrophy with wasting, weakness and fibrillation of the upper limbs, yet clearly [illegible] from the painful amyotrophy with associated sensory signs which results from the traumatically induced lateral protrusion of cervical discs described by S[illegible] and Murphy (1943) and Spurling and Scoville (1944)

The cases described here show the close clinical resemblance which may exist between certain manifestations of cervical spondylosis and those of motor neurone disease, both in its guise of amyotrophic lateral sclerosis and in that of progressive muscular atrophy

Cases Simulating Amyotrophic Lateral Sclerosis

Case 1 —A man, aged 62, was first seen in August, 1941, at the age of 50 At that time he gave six months' history of stiffness in the right leg, followed within a few weeks by stiffness in the right hand, weakness of both legs, and a tendency to spontaneous clonus on sitting down

Examination at that time revealed wasting, weakness, and fibrillation of the small muscles of the hand, right plantar response doubtfully extensor, right arm jerks brisker than left, and no sensory loss On this evidence motor neurone disease was diagnosed, but the patient was not seen again until July, 1952, when he said that his leg stiffness had remained more or less static during the intervening period, but that in July, 1951, the disability had begun to increase, and in addition he had noted some weakness and wasting of the right forearm and hand

Re examination revealed that, in addition to his spastic paraparesis and extensor plantar responses, he had developed wasting of the right arm, with fasciculation in the proximal muscles on both sides All his tendon reflexes were brisk. There was still no sensory loss In December, 1952, he was seen again and mentioned for the first time a sensation of pricking on the index finger of the right hand On this occasion a new sign of impairment to pinprick over the right index and up the medial section of the forearm was noted.

Radiography of the cervical spine revealed a slight diminution of the C5–C6 disc space, and some osteophytes (fig 1) On flexion and extension movement was normal at all levels

Other investigations —The cerebrospinal fluid (C S.F) under a pressure of 120 mm H_2O, dynamics normal, contained protein 35 mg per 100 ml, and no increase of globulin A Lange test was normal Myelography (fig 2) revealed disc protrusion not only at C5–C6 but also at C3–C4

Diagnosis —The lengthy duration of this condition, coupled with the development of sensory symptoms and signs after so long an interval, seemed to make the original diagnosis of motor neurone disease untenable, and the myelographic findings supported the view that the symptoms were due to cervical spondylosis

Treatment —A leather collar was fitted, and when he last seen the patient said that there had been some improvement in the power of his right arm and hand though the signs were otherwise unchanged.

Case 2.—A male railway worker, aged 57, was seen on March 7, 1952, complaining of stiffness of the legs and of power and control of the right hand and arm Two years earlier he had experienced dragging, first of the right leg and soon after of the left After twelve months his right hand became stiff, weak, and uncontrollable, and he had noted weakness of the muscles of the shoulder and arm. Though conscious of the flickering in the wasted muscles he had at no time had any pain or paræsthesiæ

Examination revealed blood pressure 230/140 mm Hg heart, lungs, abdomen, and cranial nerves normal, wasting of muscles of shoulder girdle bilaterally, more pronounced on the right widespread fasciculation in all the affected muscles, both legs spastic tendon reflexes very brisk arms and legs, abdominal reflexes absent, plantar [illegible] extensor, sensation normal except for diminished vibration sense in the legs

Investigations —The Wassermann reaction was negative in blood and C S F The C S F contained 2 cells per c mm and protein 55 mg per 100 ml A blood count and a fractional

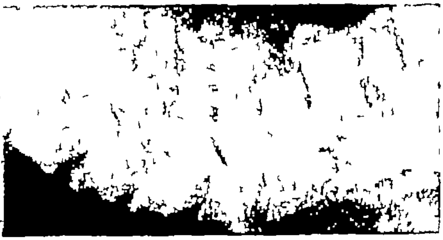

Fig 1—Case 1 : slight diminution of C5–C6 intervertebral disc space with formation of osteophytes.

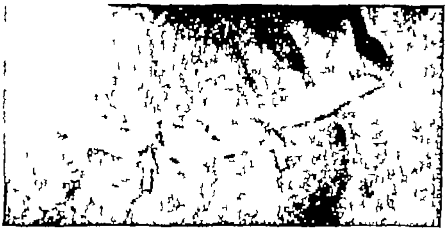

Fig 2—Case 1 : interruption of myodil pattern at C3–C4 and C5–C6 intervertebral disc spaces. Patient is prone.

test meal were normal Radiography of the cervical spine showed evidence of osteo-arthritic change Cisternal myelography revealed subluxation at C3–C4 with a break in the Myodil column A more obvious defect appeared at C5–C6

Diagnosis and treatment—On the radiological evidence the clinical temptation to attach a diagnosis of amyotrophic lateral sclerosis was easily resisted A leather collar was applied and there has been some subjective improvement in the patient's condition in the past twelve months although the signs remain unchanged There is still no pain and still no sensory change.

Case 3.—A man aged 56 was first seen in June, 1951 Three years earlier he had experienced progressive weakness of the legs. After eighteen months he noticed in addition that there was an intermittent flickering of the small muscles of the hand followed after an interval of a few months by some wasting Investigation at another hospital at this stage led to the diagnosis of motor neurone disease eminently justifiable on the evidence then available Shortly before being seen in the *neurological clinic*, however he had experienced intermittent deadness of the legs.

Examination revealed wasting and fasciculation of the transverse head of the left adductor pollicis muscle a spastic paresis of both legs and a generalised hyper reflexion. The plantar responses were extensor No superficial sensory loss was detected but there was some diminution of vibration sense in the legs. The new complaint of a sense of deadness led to his admission to hospital and on admission two months after the initial examination he had developed, in addition to his motor signs a rather patchy impairment of superficial sensation in the lower limbs His vibration sense was definitely impaired, and he made a few mistakes in position sense in the toes.

Investigations—A blood-count was normal. The Wassermann reaction was negative in the blood and the C.S.F A fractional test meal was normal The C.S.F contained 1 cell *per c.mm protein 80 mg per 100 ml* and a small amount of globulin. A Lange test was normal Radiography of the cervical spine showed pronounced degeneration of discs and osteo-arthritic lipping Cervical myelography showed indentation of the myodil pattern at C3–C4 C4–C5 C5–C6, and C6–C7 with subluxation at C3–C4

Treatment—A leather collar was fitted, and with this the patient appeared to improve a little at first In March, 1952 however he was readmitted because he said that the numbness in his legs had become more severe and he had begun to have some precipitancy of micturition. Clinical re-examination revealed a very slight increase in his signs, sensory and motor After consultation with Mr Richard Johnson skull traction was applied as a prelude to operation The patient then developed bilateral femoral thrombosis and subsequent pulmonary infarction, and his subsequent course has been a steady battle against the increasing disability resulting from the enforced immobility His collar was reapplied, with great benefit to the fasciculation and wasting in the left hand, which now appears almost normal

Case 4.—A woman, aged 60 was seen on Jan. 30 1953 complaining of weakness of the arms and stiffness of the legs Fourteen months earlier she had fallen in the street but suffered no obvious ill effects. Four months after this however she began to have stiffness in the legs, and within another month she experienced great difficulty in using her hands and arms for such activities as combing her hair and using a knife and fork. The symptoms had progressed steadily, until at the time of examination she was bedridden. There had been no pain and no other sensory symptoms She had been seen at another hospital, where amyotrophic *sclerosis had been diagnosed*

Examination showed profound wasting and weakness of the proximal muscles of the arm with slight wasting and weakness of the forearm and hand. There was intermittent fascicular twitching of all these muscles. The legs were spastic. All the tendon jerks were brisk. The plantar reflexes were extensor Vibration sense was absent in the legs; sensation otherwise normal

Investigations—A blood-count was normal The Wassermann reaction was negative The C.S.F contained 1 cell per c.mm. and protein 50 mg per 100 ml Radiography of the cervical spine showed cervical spondylosis with narrowing of disc spaces C4–C5 C5–C6 and C6–C7 and subluxation at C3–C4 Cervical myelography showed indentations in the myodil column at C4–C5 C5–C6, and C6–C7 interspaces

Cases Simulating Progressive Muscular Atrophy

Case 5—A bus-driver aged 59 was seen on Aug 17 1951 complaining of weakness, wasting and twitching of the muscles of the right arm Six months earlier he had noted flickering and jumping of the muscles of the right arm and forearm, at times so violent as to awaken his wife at night Two months later he developed difficulty in pulling the steering wheel of his bus round for a right-hand turn, and these symptoms steadily progressed. At no time had he *experienced any pain or paræsthesiæ*

Examination revealed that abnormalities were confined to the right arm and comprised weakness and wasting of all the muscles of the arm forearm and shoulder particularly of the extensors of the wrist. Coarse fasciculation was noted in all the affected muscles, but mostly in biceps and in the extensors of the wrist. The tendon reflexes were a little brisker in the right arm There was no sensory loss

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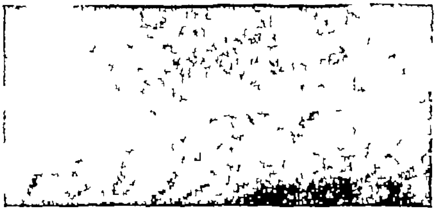
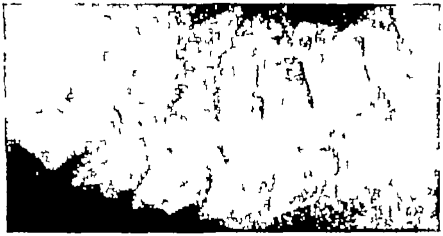


Fig 3—Case 5 : abnormality of C4–C5 C5–C6 and C6–C7 intervertebral disc spaces. In myodil pattern there is only a trickle of myodil lying in the left lateral gutter compared with good filling above and below lesion. Patient is prone



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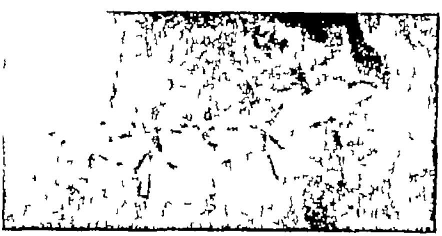

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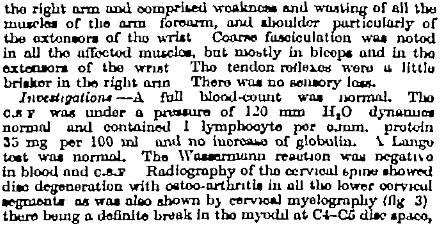

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CERVICAL SPONDYLOSIS SIMULATING MOTOR-NEURONE DISEASE

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In a large proportion of cases of cervical spondylosis sensory symptoms and signs differentiate the disorder clearly from any form of motor-neurone disease That confusion can arise, however, is shown by Brain's allusion to cases in which amyotrophic lateral sclerosis had previously been diagnosed Failure of the condition to progress led to subsequent review of these patients, and they were found to have cervical spondylosis

We have recently become aware that cervical spondylosis may also produce a syndrome closely resembling progressive muscular atrophy with wasting, weakness, and fibrillation of the upper limbs, yet clearly differing from the painful amyotrophy with associated sensory signs which results from the traumatically induced lateral protrusion of cervical discs described by Semmes and Murphy (1943) and Spurling and Scoville (1944)

The cases described here show the close clinical resemblance which may exist between certain manifestations of cervical spondylosis and those of motor neurone disease, both in its guise of amyotrophic lateral sclerosis and in that of progressive muscular atrophy

Cases Simulating Amyotrophic Lateral Sclerosis

Case 1 —A man, aged 62, was first seen in August, 1941, at the age of 50 At that time he gave six months' history of stiffness in the right leg, followed within a few weeks by stiffness in the right hand, weakness of both legs, and a tendency to spontaneous clonus on sitting down

Examination at that time revealed wasting, weakness, and fibrillation of the small muscles of the hand, right plantar response doubtfully extensor, right arm jerks brisker than left, and no sensory loss On this evidence motor neurone disease was diagnosed, but the patient was not seen again until July, 1952, when he said that his leg stiffness had remained more or less static during the intervening period, but that in July, 1951, the disability had begun to increase, and in addition he had noted some weakness and w of the right forearm and hand.

Re examination revealed that, in addition to his spastic paraparesis and extensor plantar responses, he had developed wasting of the right arm, with fasciculation in the proximal muscles on both sides All his tendon reflexes were brisk There was still no sensory loss In December, 1952, he was seen again and mentioned for the first time a sensation of pricking on the index finger of the right hand On this occasion a new sign of impairment to pinprick over the index and up the medial section of the forearm was noted.

Radiography of the cervical spine revealed a slight diminution of the C5–C6 disc space, and some osteophytes (fig 1) On flexion and extension movement was normal at all levels

Other investigations —The cerebrospinal fluid (C S.F) was under a pressure of 120 mm H_2O, dynamics normal, and contained protein 35 mg per 100 ml, and no increase of globulin A Lange test was normal Myelography (fig 2) revealed disc protrusion not only at C5–C6 but also at C3–C4

Diagnosis —The lengthy duration of this condition, coupled with the development of sensory symptoms and signs after so long an interval, seemed to make the original diagnosis of motor neurone disease untenable, and the myelographic findings supported the view that the symptoms were due to cervical spondylosis

Treatment —A leather collar was fitted, and when he last seen the patient said that there had been some ment in the power of his right arm and hand, though the signs were otherwise unchanged.

Case 2 —A male railway worker, aged 57, was seen March 7, 1952, complaining of stiffness of the legs and l of power and control of the right hand and arm Two y earlier he had experienced dragging, first of the right leg and soon after of the left After twelve months his right hand became stiff, weak, and uncontrollable, and he had noted weakness of the muscles of the shoulder and arm. Though conscious of the flickering in the wasted muscles he had at no time had any pain or paræsthesiæ

Examination revealed blood pressure 230/140 mm Hg, heart, lungs, abdomen, and cranial nerves normal, wasting of muscles of shoulder girdle bilaterally, more pronounced on the right, widespread fasciculation in all the affected muscles, both legs spastic, tendon reflexes very brisk arms and legs, abdominal reflexes absent, plantar reflex extensor, sensation normal except for diminished vibr sense in the legs

Investigations —The Wassermann reaction was negative in blood and C S F The C S F contained 2 cells per c mm. and protein 55 mg per 100 ml A blood count and a fraction

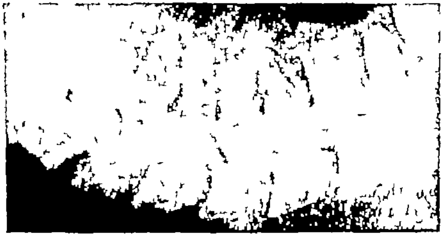

Fig. 1—Case 1: slight diminution of C5–C6 intervertebral disc space with formation of osteophytes.

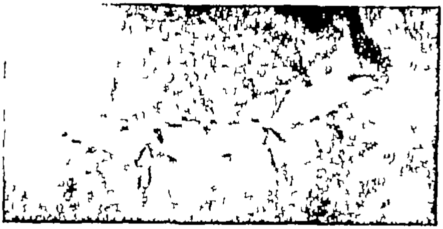

Fig 2—Case 1: interruption of myodil pattern at C3–C4 and C5–C6 intervertebral disc spaces. Patient is prone.

test-meal were normal *Radiography of the cervical spine* showed evidence of osteo arthritic change Cisternal myelography revealed subluxation at C3–C4 with a break in the 'Myodil column A more obvious defect appeared at C5–C6

Diagnosis and treatment.—On the radiological evidence the clinical temptation to attach a diagnosis of amyotrophic lateral sclerosis was easily resisted A leather collar was applied, and there has been some subjective improvement in the patient's condition in the past twelve months, although the signs remain unchanged. There is still no pain and still no sensory change

Case 3.—A man aged 56 was first seen in June 1951 Three years earlier he had experienced progressive weakness of the legs. After eighteen months he noticed in addition that there was an intermittent flickering of the small muscles of the hand, followed after an interval of a few months by some wasting Investigation at another hospital at this stage led *to the diagnosis of motor neurone disease, eminently* justifiable on the evidence then available Shortly before being seen in the neurological clinic, however he had experienced intermittent deadness of the legs.

Examination revealed wasting and fasciculation of the transverse head of the left adductor pollicis muscle a spastic paresis of both legs and a generalised hyper reflexion. The plantar responses were extensor No superficial sensory loss was detected but there was some diminution of vibration sense in the legs. The new complaint of a sense of deadness led to his admission to hospital, and on admission two months after the initial examination he had developed, in addition to his motor signs a rather patchy impairment of superficial sensation in the lower limbs. His vibration sense was definitely impaired, and he made a few mistakes in position sense in the toes.

Investigations—A blood count was normal. The Wassermann reaction was negative in the blood and the C.S.F. A fractional test-meal was normal. The C.S.F. contained 1 cell *per c.mm., protein 80 mg per 100 ml., and* a small amount of globulin. A Lange test was normal. Radiography of the cervical spine showed pronounced degeneration of discs and osteo-arthritic lipping Cervical myelography showed indentation of the myodil pattern at C3–C4 C4–C5 C5–C6 and C6–C7 with subluxation at C3–C4

Treatment.—A leather collar was fitted, and with this the patient appeared to improve a little at first. In March, 1952 however he was readmitted because he said that the numbness in his legs had become more severe and he had begun to have some precipitancy of micturition Clinical re-examination revealed a very slight increase in his signs, sensory and motor After consultation with Mr Richard Johnson skull traction was applied as a prelude to operation The patient then developed bilateral femoral thrombosis and subsequent pulmonary infarction, and his subsequent course has been a steady battle against the increasing disability resulting from the enforced immobility His collar was reapplied with great benefit to the fasciculation and wasting in the left hand which now appears almost normal.

Case 4.—A woman aged 60 was seen on Jan. 30 1953 complaining of weakness of the arms and stiffness of the legs Fourteen months earlier she had fallen in the street but suffered no obvious ill effects. Four months after this however she began to have stiffness in the legs, and within another month she experienced great difficulty in using her hands and arms for such activities as combing her hair and *using a knife and fork. The symptoms had progressed* steadily until at the time of examination she was bedridden. There had been no pain and no other sensory symptoms. She had been seen at another hospital, where amyotrophic sclerosis had been diagnosed.

Examination showed profound wasting and weakness of the proximal muscles of the arm with slight wasting and weakness of the forearm and hand. There was intermittent fascicular twitching of all these muscles. The legs were spastic. All the tendon jerks were brisk. The plantar reflexes were extensor Vibration sense was absent in the legs; sensation otherwise normal.

Investigations—A blood-count was normal The Wassermann reaction was negative The C.S.F. contained 1 cell per c.mm. and protein 50 mg per 100 ml Radiography of the cervical spine showed cervical spondylosis with narrowing of disc spaces C4–C5 C5–C6 and C6–C7 and subluxation at C3–C4 Cervical myelography showed indentations in the myodil column at C4–C5 C5–C6 and C6–C7 interspaces.

Cases Simulating Progressive Muscular Atrophy

Case 5—A bus-driver aged 50 was seen on Aug 17 1951 complaining of weakness, wasting and twitching of the muscles of the right arm. Six months earlier he had noted flickering and jumping of the muscles of the right arm and forearm, at times so violent as to awaken his wife at night. Two months later he developed difficulty in pulling the steering wheel of his bus round for a right-hand turn, and *these symptoms steadily progressed. At no time had he* experienced any pain or paræsthesiæ

Examination revealed that abnormalities were confined to the right arm and comprised weakness and wasting of all the muscles of the arm forearm and shoulder particularly of the extensors of the wrist Coarse fasciculation was noted in all the affected muscles but mostly in biceps and in the extensors of the wrist The tendon reflexes were a little brisker in the right arm. There was no sensory loss.

Investigations—A full blood-count was normal. The C.S.F. was under a pressure of 120 mm. H_2O dynamics normal and contained 1 lymphocyte per c.mm., protein 35 mg per 100 ml and no increase of globulin. A Lange test was normal The Wassermann reaction was negative in blood and C.S.F. Radiography of the cervical spine showed disc degeneration with osteo-arthritis in all the lower cervical segments, as was also shown by cervical myelography (fig 3) there being a definite break in the myodil at C4–C5 disc space

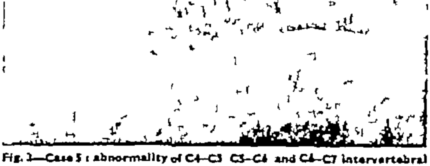

Fig. 3—Case 5: abnormality of C4–C5 C5–C6 and C6–C7 intervertebral disc spaces. In myodil pattern there is only a trickle of myodil lying in the left lateral gutter compared with good filling above and below lesion. Patient is prone.

Conclusion

We feel that, if an alternative can be devised which would involve notification of cases of true genital-tract infection only, this would encourage notification of exactly those cases for which this procedure was devised The main object of notification is to bring infectious diseases under rapid control and to prevent their spread from patient to patient the only important cause of puerperal pyrexia which falls within the scope of this objective is infection of the uterus by hæmolytic streptococci belonging to Lancefield's group A We therefore suggest that the older practice of notifying cases of uterine infection rather than puerperal pyrexia should be restored Today general practitioners are accustomed to cooperate with the Public Health Laboratory Service in the control of infectious diseases—e g, diphtheria—and it might be that confining notification to proved streptococcal cases would give more evidence of epidemiological value than does the present system

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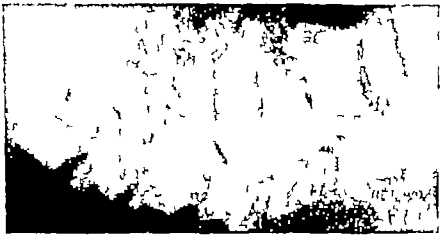

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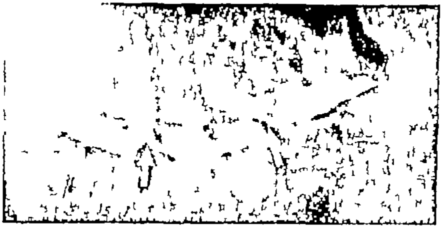

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Case 4.—A woman, aged 60 was seen on Jan. 30 1953 complaining of weakness of the arms and stiffness of the legs Fourteen months earlier she had fallen in the street but suffered no obvious ill effects. Four months after this however she began to have stiffness in the legs, and within another month she experienced great difficulty in using her hands and arms for such activities as combing her hair and using a knife and fork. The symptoms had progressed steadily until at the time of examination she was bedridden. There had been no pain and no other sensory symptoms. She had been seen at another hospital, where amyotrophic sclerosis had been diagnosed.

Examination showed profound wasting and weakness of the proximal muscles of the arm with slight wasting and weakness of the forearm and hand There was intermittent fascicular twitching of all these muscles The legs were spastic. All the tendon jerks were brisk. The plantar reflexes were extensor Vibration sense was absent in the legs sensation otherwise normal.

Investigations—A blood-count was normal The Wassermann reaction was negative The C.S.F contained 1 cell per c.mm. and protein 50 mg per 100 ml Radiography of the cervical spine showed cervical spondylosis with narrowing of disc spaces C4–C5 C5–C6 and C6–C7 and subluxation at C3–C4 Cervical myelography showed indentations in the myodil column at C4–C5 C5–C6 and C6–C7 interspaces

Cases Simulating Progressive Muscular Atrophy

Case 5—A bus driver, aged 50 was seen on Aug 17 1951 complaining of weakness, wasting and twitching of the muscles of the right arm. Six months earlier he had noted flickering and jumping of the muscles of the right arm and forearm, at times so violent as to awaken his wife at night Two months later he developed difficulty in pulling the steering wheel of his bus round for a right hand turn, and these symptoms steadily progressed. At no time had he experienced any pain or paræsthesiæ

Examination revealed that abnormalities were confined to the right arm and comprised weakness and wasting of all the muscles of the arm forearm and shoulder particularly of the extensors of the wrist. Coarse fasciculation was noted in all the affected muscles, but mostly in biceps and in the extensors of the wrist The tendon reflexes were a little brisker in the right arm. There was no sensory loss

Investigations—A full blood-count was normal. The C.S.F was under a pressure of 120 mm. H_2O dynamics normal and contained 1 lymphocyte per c.mm., protein 35 mg per 100 ml and no increase of globulin A Lange test was normal The Wassermann reaction was negative in blood and C.S.F Radiography of the cervical spine showed disc degeneration with osteo-arthritis in all the lower cervical segments, as was also shown by cervical myelography (fig 3) there being a definite break in the myodil at C4–C5 disc space

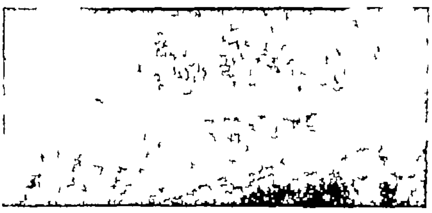

Fig 3—Case 5: abnormality of C4–C5 C5–C6 and C6–C7 intervertebral disc spaces. In myodil pattern there is only a trickle of myodil lying in the left lateral gutter compared with good filling above and below lesion. Patient is prone

and poor filling from C4–C5 to C6–C7 due to lifting of the dura by osteophytes.

Treatment.—A leather collar was fitted to this patient on March 7, 1952, and after he had worn it for only two weeks the coarse fasciculation of the arm had subsided greatly. At the end of two months there was no involuntary movement at all. The right forearm was still thin, but no fasciculation could be seen. The wearing of the collar was reduced to half days. After four months he was driving his bus normally, wearing his collar only when not on duty. When last seen on March 27, 1953, he was perfectly normal, with full strength in all muscles, and had been without the collar for three months.

This patient is of special interest for three reasons: (1) the purity of the motor signs and symptoms; (2) the extreme changes in the cervical spine accompanied by a strictly circumscribed diminution of function, in contrast to the findings in case 1, who, with scanty neurological findings, was much more disabled physically; and (3) the great benefit which can result from conservative treatment of this type of case.

Case 6.—A man, aged 56, was seen on Oct. 9, 1952, with three years' history of progressive weakness and wasting of the left hand and arm. Six months before being seen he developed some wasting of the small muscles of the right hand and had himself noticed a little twitching of the "muscles near the thumb." At no time did he experience pain or paræsthesiæ, though he had noticed some aching of the muscles of his neck if he remained in one position for any length of time.

Examination revealed that abnormalities were confined to the motor system and to the upper limbs. There was pronounced wasting of the small muscles of the left hand. The muscles of the left forearm seemed a little thinner than those of the right. On the right side there was some wasting of the interossei and there was fasciculation in the transverse head of the adductor pollicis. All the reflexes were brisk. There was no sensory loss, and the plantar responses were flexor.

Investigations.—A blood count was normal. The Wassermann reaction was negative in blood and C.S.F. The C.S.F. was under a pressure of 40 mm. H_2O, dynamics normal, and contained 1 lymphocyte per c.mm., protein 35 mg. per 100 ml., and no increase of globulin. A Lange test was normal. Radiography of the cervical spine showed osteo-arthritis with disc degeneration in the lower cervical segments. Cisternal myelography revealed a frank protrusion into the myodil column at the C6–C7 disc space consisting mainly of posterior osteophytes (fig. 4).

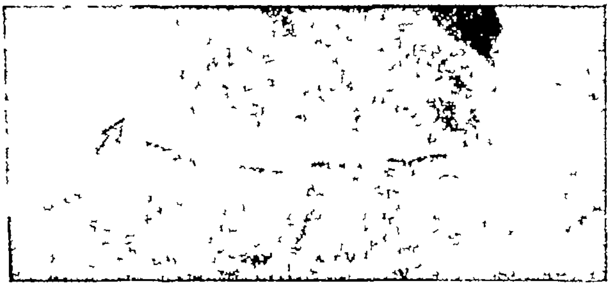

Fig. 4.—Case 6: large dent in myodil pattern at level of diseased C6–C7 intervertebral disc.

Treatment.—A leather collar was fitted to this patient on Jan. 5, 1953, and when seen on April 14 he showed great improvement. An enthusiastic pianist, he had suffered considerable disability during the development of his muscular weakness, but after the application of the collar he rapidly improved. The degree of muscle wasting was less, the power in the hand increased, and the fasciculation of the adductor pollicis had cleared. There was still some weakness of the interossei, but power was still increasing.

Case 7.—A woman, aged 45, was seen on Jan. 30, 1953, complaining of weakness of the hands. Three years previously she had experienced difficulty in extending her right index finger. After two years the ulnar three fingers of the left hand developed similar trouble, while the right hand also became increasingly clumsy.

Examination revealed wasting and weakness of both forearms, particularly of the extensor groups. There was also some weakness of the interossei, and fine movements could not be performed well. The left arm jerks were diminished and the left plantar reflex was doubtful. Sensation was normal in all modalities. Examination at another clinic led to a diagnosis of progressive muscular atrophy.

Investigations.—Electromyography revealed fibrillation potentials in the extensors of the wrists and fingers, and in the left first dorsal interosseous muscle. Radiography of the cervical region showed definite diminution of C5–C6 and C6–C7 disc spaces, with associated posterior osteophytes, and myelography confirmed these abnormalities.

Case 8.—A man, aged 57, seen on March 28, 1953, stated that twelve months previously he had first experienced difficulty in holding a golf club with his left hand. He had no pain and no sensory disturbance. After six months he noted wasting of the small muscles of the left hand, particularly in the first interosseous space. The condition had progressed slowly but steadily, and he began to notice flickering in the medial muscles of the forearm, as well as in the hand. Progressive muscular atrophy had been diagnosed before his arrival at the neurological department. His previous medical history was irrelevant, and there was no history of injury.

Examination revealed that the abnormalities were confined to the muscles of the left hand. There was loss of muscle bulk in the transverse head of the left adductor pollicis, with guttering of the hand. The hypothenar and thenar eminences were reduced on this side, and there was definite weakness of the wasted muscles. Fasciculation was seen in the transverse head of the adductor pollicis. Sensation was normal. The reflexes were brisk and equal.

Radiography of the cervical spine showed considerable disc degeneration and osteophytosis at C5–C6 and C6–C7.

Discussion

The questions raised by these cases may be grouped under diagnosis and management.

Diagnosis

The diagnostic significance is obvious, and is emphasised particularly by case 1, in whom a very reasonable diagnosis of motor-neurone disease was made twelve years earlier. The bad prognosis of motor-neurone disease is such as to discourage this diagnosis, and the knowledge that cervical spondylosis may simulate motor-neurone disease so closely leads to the careful investigation of this diagnostic possibility. Of our 8 patients 6 were male, and these, though all aged more than 50, still retained a useful position in the community. Case 1 indicates the length and type of course which may be expected in the cervical spondylotic, even without treatment—a point of considerable importance in advising patients and their families.

Management

The best course of action is not yet clearly defined. Indeed, one is tempted to suggest that no single line of therapy will ever prove to be correct for all the cases.

It seems reasonable to suppose a priori that operation in spondylosis with diffuse affection of the various intervertebral joints is unlikely to produce a very satisfactory result unless there is a very large single filling defect in the myodil pattern on myelography, and even in such cases simple excision may not yield any great benefit. The intention in case 3 (in coöperation with the department of neurosurgery) was to apply traction and then to excise the supposed projecting disc and osteophytes, but the period of immobilisation carried with it its own unfortunate sequelæ. Even in this patient, however, considerable improvement has taken place in the weak, wasted, and fibrillating left hand as a result of the application of a leather collar.

The next most active line of therapy is to apply skull traction for three or four weeks, and then to put on a Minerva plaster for from three to six months. This has certainly produced satisfactory improvement in some cases of cervical spondylosis but was not used in the present series.

The third main course open (apart from no treatment at all) is the application of a collar with breast and back plate (made of either leather or moulded plastic) This method proved very successful in cases 4 and 6 and partially so in case 3 and has been used with similar success in some of our other cases without pyramidal signs and particularly where pain was severe Bony fixation with grafts into the cervical spine has been suggested as a means of producing more permanent splinting of the affected region

Clinical Pictures

Numerous theories have been advanced to explain the diverse clinical pictures produced by these osteochondral abnormalities The concept of direct pressure of the projections upon the cord, the rootlets within the theca or the combined roots at their point of emergence through the intervertebral foramen has the appeal of simplicity and has been favoured by Spurling (1944) Spillane and Lloyd (1952), and Brain et al (1952) That this is not entirely true is suggested by the response of cases to restriction of movement of the cervical spine This improvement appears to support the alternative suggestions of direct rubbing of the cord and roots on the osteochondromatous projection (Bedford et al 1952) or else of intermittent interference with the blood supply —again by relative movements of the spine and cord— from the anterior spinal artery and its branches. In further support of this is Allen's (1952) observation on blanching of the cervical cord during operation when the neck was flexed It is quite possible that both these mechanisms are at work but in either case temporary fixation would produce improvement both of upper and lower motor neurone symptoms Our present advice to these patients is that they should wear their collars *continuously for the first three months, then wear them* only at work or at times of fairly active movement as in recreation, for a further three months We suggest that after that time the collar may be left off to await developments. Only time will show the long term value of this course

Summary

Of 8 cases of cervical spondylosis 4 displayed the clinical picture of amyotrophic lateral sclerosis and 4 that of progressive muscular atrophy

In treatment the application of a leather collar has given good results, particularly when a lower motor neurone affection is predominant

It is a pleasure to acknowledge the help received from Dr F R. Ferguson, under whose care the patients were. The radiological findings are reproduced by courtesy of Dr R G Reid and Dr C P Moxon, of the department of neuroradiology and with the help of Dr R G Ollerenshaw of the department of medical illustration

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If a city is miraculously efficient, crammed with goods bristling with services, glittering with all the latest ingenuities, but is also filled with people who are worrying themselves sick or becoming ugly minded and cruel or turning into dim robots, then that city is a flop If the people in the neighbouring country are comparatively poor have few possessions, no gadgets, no great organisations, but contrive to live zestfully laugh and love still enjoy poetry and music and talk then that country has succeeded. —J B PRIESTLEY *New Statesman and Nation* Sept 5 1953, p 251

MALARIA CONTROL IN BORNEO

JOHN McARTHUR
M.P C.S

LATE DIRECTOR OF MALARIA RESEARCH IN NORTH BORNEO SARAWAK, AND BRUNEI

JUST after the war I reported that *Anopheles maculatus* the chief vector of malaria in Malaya, was of no importance as a vector in Borneo whereas *A balabacensis* (then known as *A leucosphyrus*[*]) generally regarded as harmless in other countries was the chief and generally the sole vector throughout the greater part of Borneo (McArthur 1946)

It had been found that *A balabacensis* bred only under jungle shade and that clearance of shade and admission of sunlight led to immediate disappearance of this mosquito It was natural therefore, to suppose that clearance of jungle over breeding places of *A balabacensis* would eradicate not only this insect but also the malaria which it carried. There was a good deal of indirect evidence in support of this supposition and in view of its practical importance an experiment had been begun before the war in Tambunan, North Borneo This however had been interrupted by the Japanese occupation

PRESENT INVESTIGATION

In 1949 this experiment was again established In the selected area of about ten square miles, which was occupied by five villages the proportion of the population having enlarged spleens had averaged just over 80% in the previous thirteen years In this area the breeding-sites of *A balabacensis* were carefully defined and they were then cleared to admit sunlight by a gang of about 50 coolies working for about three months *Finally, the incidence of malaria in the area was* investigated in each of the next three years

This valley was selected partly because the prevalence of malaria in it had remained practically the same for many years and partly because it was one of the most difficult situations to deal with so that the experiment might be completely convincing

RESULTS

Breeding —The breeding of *A balabacensis* had been widespread in this valley during every examination for many years. Shortly after the clearing operations in 1949 the breeding of this mosquito fell to about 5% of its previous level, and this degree of control appears to have continued over the whole three years of the experiment without significant further work.

Enlarged Spleen —The spleen rate which had remained constant for many years in this valley was 86% just before the clearing A year after the clearing it had fallen for the first time on record to 56% and in the next two years it fell to 53% and 45% successively This reduction may reasonably be attributed to the clearing and to the control of *A balabacensis* breeding

Transmission of Malaria —Some transmission of malaria remained however as was shown by parasites in the blood of young babies This was probably due to the infiltration of infected *A balabacensis* through the jungle from surrounding highly malarious villages It is therefore extremely desirable that further work should be done over a wider area to eliminate such infiltration

Comparison Area —A very interesting finding was made in a neighbouring valley which had been selected as a comparison area In this valley the spleen rates had remained steady at 100% at every examination in thirteen years but it suddenly fell to 75% during the last survey in 1952 and for the first time on record children were then found without evidence of malaria This seemed at first to render the observations in the experimental area invalid , but an examination of the comparison area discovered the probable reason

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[*] Recent research has shown that the vector of malaria in Borneo is more correctly called *Anopheles leucosphyrus* var *balabacensis* or *A balabacensis* and this name will henceforth be used (Colless 1950)

For many years previously conditions had remained exactly the same under an elderly village headman In 1951, however, this old man died and was succeeded by a new and younger headman, who cleaned up his village, distributed drugs to the children, and applied anti mosquito measures by drainage and clearance Thus, far from invalidating the findings in the experimental area, this village proved the ability of the people to tackle malaria on their own initiative

The clearing in the experimental area lasted much longer than was at first expected, and such clearing can be maintained permanently if the people cultivate, or graze their cattle in, the moist fertile areas thus exposed Newer methods of clearing by spraying with selective herbicides—one spraying of which is claimed to be effective for five years—may prove an economical means of malaria control which is worthy of further study

CONCLUSION

This experiment, therefore, has given to Borneo a proved method of malaria eradication which is simple yet effective, economical, and permanent , which can be put into effect by the villagers , and which at the same time encourages the agricultural and economic development of the country

It is hoped that this method may be of value in all those areas where *A balabacensis* is the vector—over the hilly jungle covered country which extends from Assam in the east as far as Celebes in the west

SUMMARY

Jungle clearance with the admission of sunlight to breeding-places of *A balabacensis* led to a 95% reduction of breeding of this mosquito, and a significant fall in the incidence of enlarged spleens in an area of hyperendemic malaria

The importance of extending the area is emphasised, to eliminate the possible infiltration of infected mosquitoes from other areas

This method of malaria control is effective, economical, and permanent , can be put into effect by the inhabitants , and contributes to the health and wealth of the land

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A FOREIGN BODY IN THE ILEUM

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It is difficult to understand how a metal object almost as large as a halfpenny can be swallowed unwittingly by a person apparently sane and sober , but, as the following report shows, the thing can be done

A woman, aged 61, was sent to the outpatient clinic by Dr L Garrett with a diagnosis of subacute intestinal obstruction, probably caused by adhesions following a total hysterectomy for fibroids twelve years previously The patient stated that two weeks earlier she had been suddenly seized with severe abdominal pain and had vomited once She had had a similar attack of pain a year before, but it lasted only a few hours and she did not send for the doctor On the present occasion the pain continued to recur in colicky fashion and the doctor was summoned The patient stoutly refused to allow him to arrange immediate admission to hospital and insisted on being treated at home There was no more vomiting and the bowels acted daily, but attacks of colic continued to occur, and she finally consented to go to hospital as an outpatient

Examination disclosed only one abnormality an area, no larger than a sixpence, just to the right of the right median subumbilical scar left by the hysterectomy, where extreme tenderness was felt on pressure

Laparotomy was done two days later No adhesions were found at the site of the hysterectomy, but a loop of the lower ileum, about a foot above the ileocæcal valve, was stuck to the anterior abdominal wall at the point where tenderness had been noticed on examination When freed, this loop was felt to contain a mass which, through the intestinal wall, [illegible] an ulcer crater with very hard floor and heaped up edges Several enlarged but soft lymph glands were felt in the adjacent mesentery Search through the abdominal cavity revealed no other lesion and, supposing that I was dealing with that rarity a primary malignant growth of the small intestine, I excised about 10 inches of the loop with its mesentery and did an end to end anastomosis When, however, at the end of the operation the loop was laid open, it was found that the " ulcer crater " was formed by a saucer shaped piece of fine mesh wire gauze 24 mm in diameter, probably part of a tea strainer This lay in the long axis of the bowel and had produced ulceration at two points on the mesenteric and antimesenteric borders of the much thickened wall of the bowel On the antimesenteric border the ulceration had involved the muscular coats and caused adhesion of the loop to the abdominal wall

The patient made an uneventful recovery She learned with surprise of the foreign body and was quite unable to remember any occasion when she might have swallowed it, which she probably did shortly before the attack of pain a year previously

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Preliminary Communication

DIMINISHED URINARY EXCRETION OF CITRATE DURING DEFICIENCIES OF POTASSIUM IN MAN

The method of Hargreaves et al[1] has been used to measure the rate of excretion of citrate in the urine and the concentration of citrate in peripheral venous plasma during states of potassium deficiency Most of the observations were made during the course of the deficiencies of potassium induced in two normal men (A and B) by the ingestion of a cation exchange resin and of a diet containing little potassium (cf Fourman and Ainley-Walker[2])

Total deficits of 300 and 450 m eq of potassium were achieved in the two men, who experienced general malaise, loss of appetite, and constipation but were not severely ill After the administration of the resin had been stopped, small amounts of potassium were retained from the diet, but the deficits were not completely made good until extra potassium had been given There was a moderate extracellular acidosis while the resin was being administered, but this was rapidly corrected afterwards by the absorption of sodium, some of which entered the cells

The urinary excretion of citrate was also measured in a woman, aged 44, with renal acidosis who was losing excessive amounts of potassium in the urine

RESULTS

The accompanying table shows that during the control period A excreted about 160 mg , and B about 380 mg of citrate a day They excreted only 38–70 mg a day when they were deficient in potassium, and the amounts were independent of the acid-base balance in the plasma and of the urinary pH The excretion of citrate remained low when 96 m eq of potassium was administered daily as the citrate and did not return to its control value until the deficiency of potassium had been completely made good The low urinary excretion of citrate was not associated with a demonstrable fall in the plasma citrate level and therefore was presumably renal in origin.

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[1] Hargreaves, C A Abrahams M. D , Vickery, H B *Analyt Chem* 1951 23, 467

[2] Fourman P , Ainley-Walker, K. M S *Lancet* 1952, ii, 368

The woman with renal acidosis had a plasma bicarbonate level of 15 m eq per litre, and her urinary pH was 7 3–8 0 She excreted 4–74 mg of citrate daily and did not excrete more when she had been given 15 g of KCl daily by mouth for some time. It is not yet known whether her deficiency of potassium can be corrected in this way

URINARY EXCRETION OF CITRATE

Period	Day of expt.	Total K deficit (m.eq)	Plasma CO_2 (m.eq per litre)	Urine pH	Urinary citrate (mg per 24 hr)
Subject A (age 26 weight 56 kg)					
Control	0–4	0	27	6 7	108
	4–8	0	28	6·5	118
With resin	8–12	280	17	5 7	38
	12–16	330	23	6 1	72
After resin	16–18	270	29	6 1	45
	18–20	200		6 4	42
K citrate added to diet	20–21	80		6 7	64
	21–23	0	31	7 4	116
Subject B (age 29 weight 7 kg)					
Control	1	0	28	5 9	410
	5	0	27	6·0	353
After resin	14	390		6·0	57
	15	360	22	6 2	69
	16	330		6 4	66
	17	300		6·6	105
	18	270	30	6 7	123
K citrate added to diet	19	145		6·0	66
	20	15		7 3	275
	21	0	27	7 4	300

DISCUSSION

The quantity of citrate normally excreted is 0 20–1 0 g It varies inversely with the concentration of hydrogen ions in the urine, but citrate is so completely metabolised that the urinary output bears little relation to the dietary intake[3] Our results have disclosed that during a potassium deficiency the rate of excretion of citrate may become low and remain so even when the urine has been made alkaline by the ingestion of citrate. The precise functions of potassium in cells are uncertain, but any connection between the most abundant intracellular cation and an intermediary in the tricarboxylic cycle through which most of the aerobic metabolism of the body is mediated is of interest It may be noted that the metabolism of glucose becomes depressed by a deficiency of potassium[4] These preliminary results suggest that further investigations of the metabolism of citrate during potassium deficiency are desirable

SUMMARY

The urinary excretion of citrate was measured in two normal men before during and after an experimental deficiency of potassium

The excretion of citrate was diminished while the men lacked potassium

It was also diminished in a patient with renal acidosis and potassium deficiency

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Department of Experimental
Medicine University of
Cambridge

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Clinical Tropica

A. R D ADAM
department; B
professor of tropica
Medicine Oxford
1953 Pp 508 40s

A NEW book on tropical
as coherently constructed
authors have confined thems
physician and the pathologist
see them in hospital for there ... ore
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dispensary or field unit of the trop ... iberately
avoid discussion of the parasites an ... —details of
which are readily available in oth ... oks—and say little about prevention and control These are self imposed restrictions; and the book within its chosen scope is admirable The writing is clear terse and intentionally dogmatic as students like it. Subjects are taken alphabetically—ainhum first and yellow fever last—with the odd result that in the middle between melioidosis and mycetoma pedis, there is a chapter on miscellaneous worm infestations.' Blackwater fever under this arrangement, is a far cry from malaria; but this does not matter since the ætiology is made perfectly clear The authors have included a surprisingly large amount of modern and important information—though the account of Q fever could be expanded This first-class book can be strongly recommended to clinicians

The Liverpool school has already produced a textbook of parasitology, there now remains the need for one on tropical hygiene, in which the diseases of people living in the tropics can be studied in relation to their background

The Neuron

Organiser: M. DEMEREC Symposia on Quantitative Biology Cold Spring Harbor Vol 17 1952 Pp 323

THE display of experimental ingenuity and inductive virtuosity contained in many of the papers included in this volume is impressive. A glittering array of neurophysiological authorities—Lorente de No Bodian, Bronk, and, from the non American world, Eccles Monnier, and Hodgkin—met last year to share their knowledge and stimulate their ideas on the neurone by discussing the properties of nerve axons the peripheral origins of nervous activity and the neurone soma and its electrophysiological properties as well as to review cortical, spinal, sympathetic and junctional nervous activities These discussions were for the most part rather speculative and the speakers are at some pains to confess the possible defects of their conjectures.

There is a neat contribution by C R Skoglund on the chemical factors modifying transmission through the cat s spinal cord. Few will fail to be impressed by the lucid realism of David Bodian s introductory survey of neurones the directness of A. L. Hodgkin and A. F Huxley in their discussion of sodium and potassium ions during nervous activity and the uncontested ingenuity of J C. Eccles in evolving a neuronal model which appears to explain much of the behaviour of motor neurones in experimental investigations.

All will come to understand the neurophysiologist s debt to that benign providence which placed in the waters of the earth the squid with its giant nerve-fibres.

Gynecological and Obstetrical Pathology

PETER A. HERBUT M.D professor of pathology, Jefferson Medical College Philadelphia. London: Henry Kimpton. 1953. Pp. 683 93s 6d

THIS is a carefully compiled book. For each subject in turn Dr Herbut has studied several recent reviews and fused them to form a short compendium of modern knowledge

This method is very successful with topics of which he obviously has extensive personal experience for this enables him to select his reviews well, and assess the evidence critically On topics with which he is not so familiar however he lacks the confidence to differentiate the traditional from the true and gives lists which could have been assembled almost as

Most of the standard gynæco
on record children were th with, and, in addition, information
of malaria This seems of rather esoteric conditions such as
tions in the experi the cervix, blastomycosis of the uterus,
tion of the coma of the fallopian tubes The sections on
reason uloma and on granuloma inguinale are well done,
For ere is a full and useful chapter on the placenta The
chapter, on "The Mother," not by Dr Herbut, is below the level of the rest of the book

In this country there is a tradition that pathology is to be studied only through the mortuary, the museum, and the microscope This book shares the broad outlook of several other American textbooks, where pathology is interpreted as the scientific study of disease in all its aspects—disturbances of function as well as of structure, reasons for characteristic signs and symptoms, specific lines of treatment, and prognosis

Clinical Electrocardiography

Textbook for Practitioners and Students MAX HOLZMANN, Zurich, translated by DOUGLAS ROBERTSON, D M, M R C P London Staples Press 1952 Pp 647 105*s*

Prof Holzmann's book is not for the beginner, but for the advanced student, research-worker, and experienced cardiologist

The electrophysical basis of the electrocardiogram obtained by limb and chest leads, and the methods and theory of vectorcardiograms, are thoroughly considered Œsophageal and intracardiac leads are also dealt with, but briefly The important and sometimes overlooked effects of posture, exercise, and other physiological stresses on the picture are well set out Passing to the abnormal, the auriculogram and axis deviation are discussed in unusual detail The section on the electrocardiogram in the various grades of myocardial ischæmia is adequate though not so full, considering its importance, as some other sections, and perhaps there is too much insistence on exercise tests There are a few printer's errors, and the style often recalls that this is a translation

The book throughout is hampered by a Germanic thoroughness which makes it heavy going, but it is a work of the first importance

The Sensory Order

An Inquiry into the Foundations of Theoretical Psychology F A HAYEK, professor of social and moral science, University of Chicago London Routledge & Kegan Paul 1952 Pp 209 18*s*

FEW psychologists would have the courage to venture as deeply into economics as Professor Hayek here does into psychological territory In the preface he explains that as a young man hesitating between economics and psychology, he conceived some basic ideas about mind as a particular order of symbolic events, these he has developed into the present work, based not upon experiment and direct observation but on reflection, reading, and the experience of a student of social theory The outcome, necessarily speculative and philosophical, takes less account of recent developments in neurophysiology than the thesis requires, concerned as it is with the whole of the neural events which accompany sensory experience It is nevertheless a notable contribution to the theory of perception, and it adds a footnote to the mind-body problem while denying "any ultimate dualism of the process governing the realms of mind and that of the physical world respectively," Professor Hayek recognises that "for practical purposes we shall always have to adopt a dualistic view"—a seeming inconsistency which he defends in his final chapter on "Philosophical Consequences"

Storming the Citadel

The Rise of the Woman Doctor E MOBERLY BELL London Constable 1953 Pp 200 18*s*

MISS Moberly Bell has written a very entertaining and at times exciting account of the rise of the woman doctor, and the foundation and development of the Royal Free Hospital School of Medicine In the main it is concerned with the early struggles, disappointments, and final triumphs of Elizabeth Blackwell Elizabeth Garrett, and Sophia Jex-Blake The debt of all medical women to these three, and in particular to the last, can hardly be overestimated She alone had the imagination to see the immense value of a school of medicine run for and by women Yet when the school had begun it was realised that she was temperamentally unsuitable for the post of secretary which she longed to hold Sophia never showed more finely the essential generosity of her spirit than in the way she took this bitter disappointment she left London and returned to Edinburgh, the scene of her earlier struggles But she would have been more than human had she been equally generous when Elizabeth Garrett Anderson was about to be appointed dean, for Elizabeth had opposed the foundation of the school Moreover she believed—unjustly—that it was Elizabeth who had prevented her from becoming secretary She returned to London to record her dissentient vote, but Elizabeth was elected, and that was the end of any pleasure Sophia could take in the London School of Medicine for Women

The male reader cannot but feel ashamed at the outrageous way his forbears treated these aspiring women, but that should not lessen his interest and delight in an unusually readable book Medical women will read it with pride, and with gratitude to the small band of very courageous women Both will agree that it is well that such energy is no longer dissipated in a fruitless struggle between the sexes

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Functional Disorders of the Foot *Diagnosis and Treatment* (3rd ed Philadelphia and London J B Lippincott 1953 Pp 345 52*s*) —The appearance of a third edition of this little book by Prof Frank D Dickson and Dr Rex L Diveley is evidence of a call for it, and the personal popularity and high reputation of its two authors on this side of the Atlantic will certainly enhance its appeal in this country Some new material on architectural defects of the bones of the foot as a cause of foot imbalance and on other subjects has been added, and the chapter on rigid flat-foot has been rewritten to embody the fine work of Harris and Beath On the whole it is a valuable book, particularly in the emphasis laid on acquiring stability and balance in the foot of the child and adolescent Some of our own shoemakers might take to heart the comments made on the proper design of footwear, even though the authors apparently accept as inevitable that correct principles must give way to "style" when years of indiscretion are reached This book has the weakness of being highly repetitive, not always for the sake of accentuating the point at issue Some of the statements (e g, that "calcium and phosphorus deficiency are unquestionably the underlying cause in most cases of knock knee and bow legs") are questionable, and excision of os calcis spurs has long been abandoned in this country as giving no benefit Not all the illustrations are of high quality Nevertheless, the emphasis of the book is all on the clinical and functional side, and it has already succeeded in its main design "to stimulate the interest of the medical profession in disorders of the feet"

Trusts and Foundations (Cambridge Bowes & Bowes, 1953 Pp 194 42*s*) —Compiled by Mr Guy Keeling and edited by Mr Thomas Landan, this is a pioneer attempt to provide a guide to grant making bodies It is not a comprehensive survey by any means as Mr Keeling says in his preface, only the Government would be in a position to make that There are 110,000 known trusts and foundations in England and Wales alone, and the actual figure is thought to be even higher This guide only deals with some 1000 scattered through Great Britain and the Commonwealth Lord Nathan, in a foreword, mentions the inconvenience caused to would be beneficiaries by the lack of full and precise information about such trusts, and describes the book as an illuminating cross section It gives details of the purpose and conditions of all the trusts listed, and carries a classified index, an appendix on Government grants to voluntary agencies, a bibliography of sources of information, and several blank pages for notes The publishers intend to issue further editions incorporating additional information This looks like the beginnings of a very useful service indeed

Symposium on Fatigue (London H K Lewis & Co 1953 Pp 196 24*s*) —In March of last year the Ergonomics Research Society held a symposium on Fatigue, of which we published a report (*Lancet*, 1952, i, 868) Many of the papers read then have now been brought together in a book, well printed and illustrated, with a foreword by Mr W F Floyd, PH D, and the Rev A T Welford, who have edited it All those working on this perplexing subject will be glad that this material has been published

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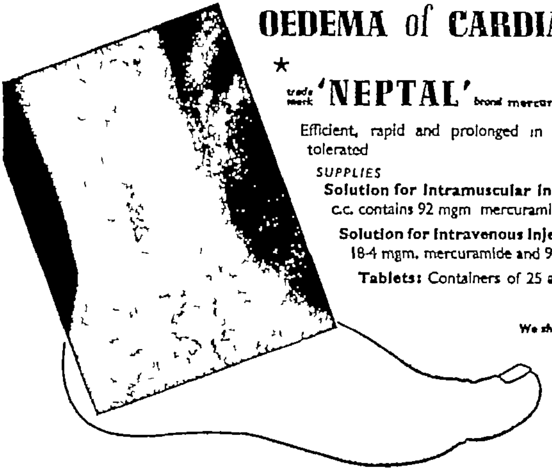

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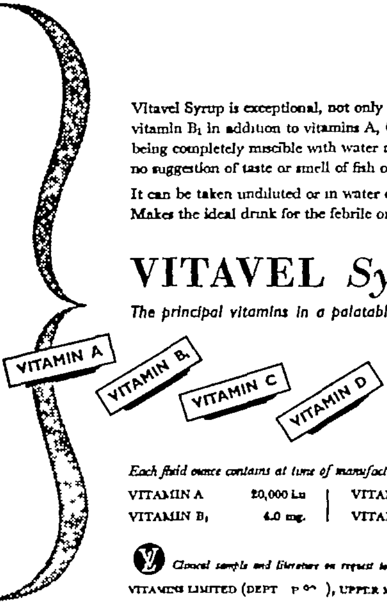

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THE LANCET

LONDON SATURDAY, SEPT 26, 1953

General Practice

THE *British Medical Journal* this week publishes a mass of new material on the state of general practice in this country, together with an analysis of the opinions of practitioners on the work they are doing. A committee of the British Medical Association, with Dr C W WALKER as its chairman, presents recommendations which are chiefly aimed at bringing practitioners into closer relation with the hospital and public-health services and which are important to all sections of our profession because they are a major attempt to counter the tendency to its fragmentation.

The journal opens with a report by Dr STEPHEN HADFIELD, an assistant secretary of the B.M.A., on the observations he made personally on 188 practices in each of which he spent the best part of a normal day between February, 1951 and March, 1952. Unlike Dr J S COLLINGS, whose disturbing "reconnaissance had lately been described in our columns,[1] Dr HADFIELD was in a position to take a cross section of the entire body of general practice in Great Britain instead of selecting a number of more or less representative types of practice he was able to compile a more comprehensive sample—the initial list being formed by taking every 64th name in the list of practitioners in each region. Necessarily, as in the Collings survey, his approach was critical 'in the hope that the discovery and assessment of shortcomings faults, and difficulties might lead to action which would eliminate them' but his forbearing judgments are less emphatic and he is evidently not concerned to convey the same urgent impression of widespread deterioration in practice for lack of proper facilities to do good work. But what he saw was not perhaps very different from what COLLINGS saw. At the time of his survey he says, 49% of practitioners had premises adequate for maintaining a high clinical standard and 17% had premises which were more than adequate but in 24% something essential was missing and 10% were unsuitable. (He rightly adds that "while present housing conditions prevail a knowledge of the facts is necessary before premises are criticized.) His comparative satisfaction with equipment ("on the whole the standard is quite adequate as to essentials") is somewhat offset by his remark that many practitioners have electric sterilizers and those that have not usually have available some method of sterilizing instruments'. Facilities for examination, such as an examination couch, were missing from 11 surgeries, and Dr HADFIELD was surprised at the prevalence of the method of examining the abdomen through the clothes and with the patient standing. A statement that at least 60% gave all their patients what examination was necessary does not again, entirely restore confidence shaken by the previous observation that 93% *of the doctors he watched at work made* 'some sort of examination in some cases". A quarter of them he thought, seemed to pay rather scant attention to record keeping, and only about half had some form of secretarial or clerical help suited to their needs. We bring out these less favourable findings from the survey because we think it should be fully understood that the conditions under which practitioners are obliged, or have accustomed themselves to practise are still quite commonly defective in ways that can and must be put right. Dr HADFIELD found that in a substantial proportion of practices lack of time had reduced the range of service the doctors could give their patients, but he felt that the large majority would not allow their work to be so hurried as to interfere with its quality. Though with more work there was less time for friendly converse only 6% of the practitioners visited regarded their relationship with their patient as a purely matter-of fact or business-like one nearly all were ready to give helpful advice on health and preventive medicine when asked by the patient and about nine out of ten regarded the giving of non medical advice as a part of their calling. In view of contrary statements it is good to note that most of the doctors visited were anxious to keep in close touch with patients receiving hospital treatment that the majority showed an interest in the family and occupational background of the patient and that 96% believed that if possible the doctor should really be a family doctor, attending the whole family. It is encouraging, too to read that, even in those financially darker days of 1951–52 a large body of the profession could be described as receptive towards the N H.S ready to like it more and more and determined that a good service shall evolve with full benefit for the patient and contentment for the general practitioner'.

Dr HADFIELD had a series of questions which he regularly put to the doctors he visited, and his report summarises the replies. To supplement this personal interrogation the General Practice Review Committee on July 12, 1951 posted similar *questions* to the rest of the general practitioners in the country whose voices, as it said, might not otherwise be heard. To make the questionary less formidable and promote fuller answers, it divided the practitioners into groups of 450–500, each of which got only two questions, and in the end it obtained facts and comments from 12 657 doctors (72% of the possible response). Belonging as they do to the pre-Danckwerts period some of these facts and comments are out of date, but others remain at least as significant as they were two years ago. What is chiefly evident from them is the impossibility of reviewing the activities of general practitioners usefully without also discussing the habits of a great many other people, such as consultants housemen ward sisters administrators midwives health visitors medical officers of health the writers of medical articles in the popular press —and of course patients and their relatives. In a service that claims as one of its biggest achievements so far the wider distribution and greater accessibility of specialists it is discouraging to read so much evidence of the frequent failure of consultants —especially among the younger generation—to give

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1 *Lancet* 1950 i, 555 547

the practitioner the help he really needs It is not always easy to remember, or even believe, that what is in itself a highly efficient and skilful specialist unit or service may fall far short of success when looked on as part of comprehensive medical care, and in considering how far he is making the practitioner's work easier, or more difficult, every consultant will do well to ponder the many passages in this report that express disappointment with hospitals Here are two—one tolerant and one severe

> "The difference is subtle and hard to define I am still on the very best of terms with our local consultants, as before, but somehow there is a difference In the old days one used to ring them up constantly and discuss cases and people Now one feels they are no longer dependent on us, and they seem to be so much taken up with clinics here, there, and everywhere, and somehow one doesn't like to bother them"
>
> "Many consultants now exercise much less care or even courtesy in reference to the practitioner The patient's confidence in his own doctor is of much more value to him in the long run than the occasional 'cleverness' of a consultant This confidence is in the best interest of the patient and should be fostered and not destroyed"

Confidence is destroyed in another way by the hospital which does not get in touch with the practitioner at once when his patient is discharged or even when his patient dies Here as elsewhere it is failure of contact that is the trouble, and the same failure is seen all too often and all too plainly between practitioners and public health doctors ("having been in practice here for the last 40 years, I have never even met my three district M O H S") "My foremost impression," Dr HADFIELD says, "is that of lack of unity in the N H S and lack of unity in the medical profession The human gaps must be closed The general practitioner, the consultant, and the public health medical officer need to get to know each other and then to learn to work in concert"

In its recommendations the committee lays less stress than some of us on the development of group practice, though it welcomes the tendency of practitioners to associate for their work Its main desire is to bring general practice into closer relation with public health on the one hand and hospitals on the other, composing the differences and closing the gaps between the three branches of the N H S, for "medicine must be practised as a unity" The practitioner can and should work more happily and advantageously than he usually does with the M.O H, the clinic doctor, the midwife, the health visitor, and the district nurse At the hospital he should have direct access to pathological and radiological departments, he should be able to perform minor surgery, he should have beds wherein to conduct confinements, and others where he can treat patients for "general-practitioner" conditions, he should hold clinical assistantships, and he should be a welcome visitor in the wards The patient whom he refers to a particular consultant should not be seen by an assistant unless the consultant expressly delegates this duty, and in emergency the hospital to which he normally sends his cases should share with him the onus of finding a bed for his patient With all this we strongly concur But in the further suggestion made to the committee, "that, just as every patient has his own doctor, so every practitioner sh have his own hospital" we see need for caution The risk is that, in seeking to overcome the isolation of general practice we may end b turning the practitioner into a peripheral and subordinate officer of the hospital service What, on the contrary, we ought to do, and must see that we do, is to strengthen his position as the person primarily and permanently responsible for the patient In a time of inevitable specialisation, the general practitioner alone has the opportunity to care for the patient as a whole, and it is for this difficult duty that he must be better armed

Cardiac Output and the Position of the Patient

WHEN those brought up in the clinical tradition believe that a quantitative method will provide an answer to the important questions that they are asking themselves, it is not surprising that they are sometimes carried away by the figures and ignore the ordinary precautions of quantitative work and the limitations of our present knowledge Thus it satisfied many to note that cardiac output fell by as much as a third when the recumbent was changed to the upright posture,[1] [2] for then the practice of nursing cardiac patients in a sitting position was confirmed and hallowed by the experimental method Cardiac catheterisation is now so universally practised that it is perhaps surprising that no planned experiment has been undertaken until recently to te the repeatability and to check the errors of a singl estimate of cardiac output The paper by DONAL et al[3] is, therefore, a particularly important significant contribution to our interpretation laboratory findings

Many factors, both known and unknown, combine to vitiate the results obtained in man (in none are these so numerous as in those medical knowledge) To enable comparisons to made either between repeat estimations in same patient or between different patients, it h become essential to minimise the effect of these fa by ensuring that the subjects of the experiment in a "steady state" and that both the procedur adopted and the accuracy of the methods used shoul be clearly defined DONALD and his colleagues carefully planned their work to this end The precautions and the steps taken to attain the steady state admirably set out and might well be taken as standar practice in any investigation requiring accurate stud of cardiac output Even with these precautions, th difference in cardiac output between two succ estimates taken at an interval of approximately minutes may be as much as 1 75 litres per min although in the majority of instances it was much Indeed, in those patients with a high output, difference of 0 1 vol. % in the A-V difference may reflected as a half-litre difference in the card output For the whole series the standard error of single estimate of cardiac output was approximate 8%—a finding essentially similar to that obtained COURNAND[4] from a selected, though not comparable, series of patients

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1 McMichael J Sharpey Schafer, E P *Brit Heart J* 1944 6

2 Stead E A jun Warren J V, Merrill, A. J, Brannon E *J clin Invest* 1945 24 326

3 Donald K W Bishop J M., Cumming G, Wade O L C Sci. 1953 12 199

4 Cournand A. *Fed Proc.* 1945, 4, 207

Having established the quantitative measurements on a sound basis DONALD and his colleagues then provided data from which the effect of nursing positions upon cardiac output could be determined. It is pleasing to see published data from which the reader can draw his own conclusions and compare them with those of the authors—a practice which might with advantage be more frequently followed. They found that the effect of posture on the cardiac output was variable. In some subjects cardiac output remained unchanged, in some it rose, and in some it fell. In the whole group there was a mean decrease of 0·36 litre per min.; this decrease was statistically significant, but the authors consider it to be so small as to be probably unimportant. The 36 people studied included 10 normal subjects, 6 with a high resting cardiac index and 6 with a low cardiac index, 6 patients with mitral stenosis, and 8 with either cardiac or respiratory disorders. In a heterogeneous clinical group the mean results may bear little relation to the clinical significance of the findings in the various subgroups, and in selecting their subjects to cover all variables, DONALD et al. have necessarily had some difficulty in expressing their results, even though none of these subgroups behaved differently from the whole group. It is conceivable, for example, that in the group of patients who had lately been in congestive cardiac failure the work of pumping 0·36 litre per minute extra—500 litres per day—might be quite sufficient to cause the death of a patient on the borderline of congestive failure, if he was nursed flat—an unlikely event. The renal tubules excrete excess sodium long before changes can be detected in the plasma, and life is sustained on one or two microgrammes of vitamin B_{12} daily. It would not be surprising, therefore, if the body's homoeostatic mechanisms in the cardiovascular system were more sensitive than the present means of measuring them. If this is so, then it is unlikely that statistical analysis in a heterogeneous group can reflect the true state of affairs unless the number of subjects in the subgroups is greatly increased. This in the matter investigated by DONALD et al., would entail Herculean work out of proportion to the importance of the question posed—and these observations are applicable to many aspects of clinical research. DONALD and his colleagues have appreciated the difficulties and they have been conservative in interpreting their findings concerning cardiac output in direct relation to clinical problems.

That the measurement of cardiac output is at present rather crude is also suggested by the more consistent findings with pulmonary artery pressures and pulse pressures—measurements that are subject to smaller error. DONALD et al. found that in the sitting position the pulmonary artery pressures, in people with a high initial pressure, and the pulse pressures in the whole group fell. While it is readily understandable, though by no means proven, that symptoms are relieved by a fall in pulmonary artery pressures and by the consequent decrease in the demands on the heart, it is hard to understand the teleological reason for the fall in pulse pressure in the sitting position in normal subjects, seeing that most of us sleep flat. No doubt much more evidence will be forthcoming to answer these questions, but meanwhile the clinician may be relieved to know that it is justifiable to nurse his patients in the position they find most comfortable.

The Public's View of Tuberculosis

SURVEYS of public opinion, ranging from the housewife's view of foaming detergents to the mother's estimate of child welfare clinics, are as popular as ever. GORE and HARTSTON[1] have now given the results of a survey, made during the first quarter of 1952 by health visitors, of 1080 mothers of children born in the administrative county of London and in Tottenham during the fortnight ended Sept. 1, 1951. The aim was to measure the extent of the public's knowledge of pulmonary tuberculosis and to see whether people were aware of the facilities for the diagnosis and treatment of this disease. The inquiry was made among a readily accessible group of women who were to some extent selected in that they were the mothers of six-month-old babies and represented, therefore, only a small proportion of the whole female population. An earlier survey, carried out in the London area in 1950, was partly based on a questionary about tuberculosis which was put to 432 adults, a carefully selected "random" sample. This inquiry was also used to compare the reliability of those interviewers who were fully experienced in the technique of interviews with that of interviewers new to the work. An analysis showed that the responses obtained were sufficiently close to justify the use of amateur interviewers when these were easier to come by.[2] This finding is of importance when judging the results of the surveys made by students from the teaching hospitals as part of their public-health training—for example, a recent survey to assess the value of antenatal instruction and child-welfare clinics.

The tuberculosis questionary used in 1950 was used again by the health visitors in 1952. The first question dealt with the relative mortality of tuberculosis and cancer; 44% of those interviewed thought that tuberculosis killed most people in this country, and 35% considered cancer to be the chief cause of death. At the time of the survey 41% thought more about tuberculosis than about any other disease—nearly twice as many as those whose thoughts were more often on cancer. It should be noted that the early part of 1952 was not a time when poliomyelitis was *prominently in the public mind*. The confusion about tuberculosis is indicated by the fact that while 43% thought that the disease was hereditary, 44% believed it was not; and of those who said that it was not or did not know, 42% had no idea how the infection could be conveyed. Contrariwise, when asked if the disease was catching or contagious 71% said "yes" and 22% said "no". Of the 1080 women interviewed 66 said that there was somebody with tuberculosis in their family at the time, but 30% of this contact group did not think that the disease was infectious. This figure makes it clear that the instruction given by tuberculosis health visitors and chest physicians is not getting across or is being misunderstood by patients and their families. But 80% of the 66 women who were family contacts said that their chests had been radiographed, which indicates very efficient supervision of contacts either by mass X-ray units or by chest clinics, though 80% is probably

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1 Gore, A. T., Hartston, W. *Mon. Bull. Minist.* *Serv.* 1953, 12, 131.

2 Durbin, J., Stuart, A. *J. R. statist. Soc.* 1951

higher than the proportion in the whole contact population. Few physicians at chest clinics would claim a supervision-rate as high as this The failure to examine all contacts may be partly explained by the fact that 69% of the women questioned thought that many people were afraid to be examined in case they had tuberculosis The sketchiness of the public's knowledge of tuberculosis was also shown by the finding that 54% of women knew nothing about the causes of extrapulmonary tuberculosis, and only 4% suggested that milk had something to do with it In several other ways the survey disclosed lack of information or failure to absorb it 80% had never heard of B C G vaccine, more than half realised that hospitals and sanatoria were provided for treatment, but only a quarter knew that priority food and milk were available for tuberculous patients On the other hand, 72% said that the present number of hospitals and sanatoria was insufficient to deal with a disease which 91% considered to be a serious problem and which 61% thought was more serious than poliomyelitis These results are very similar to those obtained by DAVID[3] in his analysis of the 1950 survey, with one curious exception in the answers to the question about symptoms Frequent cough was thought to be a symptom by 63% of the mothers and by only 35% of those in DAVID's analysis, 19% mentioned blood in the sputum, as compared with 8% in 1950, and 28% included loss of weight, as against 18% in the earlier figures Perhaps this difference was the result of direct questions at the antenatal clinic, but it may also be attributable to the valuable health teaching given by certain women's magazines

When, as the survey suggests, 80% of this adult population know where to go for an X-ray examination of the chest which 98% feel should be done regularly to combat a disease which 80% think is curable, which 91% believe is a serious problem to the country, and which 71% know to be contagious, it is disappointing that the spread of the disease has not been checked more rapidly Can it be because of the 69% who are afraid to be examined in case they have the disease? Or is there some error in the survey—not in the sampling, but in the method of interview? There is now some evidence from the interviewers, both amateur and professional, that the much-interviewed public, especially the housewife, is at last beginning to show some "interviewer resistance" No longer are questions answered with a simple spontaneity, but with some hesitation as if the speaker was considering whether or not the answer would please the interviewer, or weighing any indirect repercussions that might arise from the reply So it is becoming increasingly difficult to be sure that figures obtained in this way accurately reflect public knowledge and opinion But these latest results emphasise the importance of vigorous propaganda, and the best keynote in the campaign is the cheerful one that patients *can* be made well and restored to a normal life Using all the well-tried methods of advertising, backed by instruction through the press, radio, television, and cinema, the methods of prevention and the importance of early treatment can be driven home Although modern chemotherapy has greatly improved the chances of successful treatment, it has not detracted from the importance of knowledge as a means of prevention

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[3] David, S T Tubercle Lond 1952 33 78

Annotations

THE MEANING OF EDUCATION

THE hours we spent with dogfish and club moss nerve-muscle preparations, test tubes, cultures, microscope slides laid down in us patterns as lasting those in Pavlov's dogs Even if we have since be exponents of the art, rather than of the science, medicine our training has preserved in us some linger sense of proportion and discrimination when the scienti aspects of our calling are discussed This is something but as a preparation for life was it enough? Was i even thorough enough, let alone wide enough? D A T Macqueen[1] thinks not, and he urges the val of philosophy as a mind-widening discipline for student "Despite the lip service paid to the concept of tr the patient as a whole," he says, "too many med students graduate with the idea—which their teache do little to correct by philosophical teaching—that ma is little more than a collection of basic particles, built into cells and organs, which needs occasional techni repair and a lot of humouring" There is no cohere theory of medical philosophy, yet (as academic phil sophers are always trying to point out) all men a applied philosophers, none more so than doctors, every decision, every word of advice given by doct implies a philosophy, an attitude to man, to human and duties, and to the universe as a whole If do themselves have no clear notion of their philosophy diverse and random impressions must they leave their patients, and what vast tracts of their pat minds and natures they leave unexplored

The idea of learning philosophy—and its companion, logic—does not readily commend itself doctors Scientific method, we are apt to think, is should be—a better training for the mind than logic was As for the relations of man to God and the unive and all that, the attitude proper to a scientist is cism In modern education, however, and espe perhaps in medical education, the opportunities hearing what great minds in the past have thought ab such topics are so few that our attitude of might strike an informed observer as one of Medical ethics are no more self-evident than any kind of ethics What is a "right" or a "wrong" (or professional) act? This is a problem in app philosophy, yet our universities seem to assume that medical student can solve it without formal or any encouragement to consult published Certainly many doctors (like many other univ students) cannot distinguish between a primary and secondary cause, and here Dr Macqueen refers us examples to *The Lost Tools of Learning*,[2] a paper read Miss Dorothy Sayers to a vacation course in ed few years ago She illustrates not only such failures discrimination, but also the common trick of ass the thing we set out to prove Modern education, argues, does not teach us how to learn we rem what we have learnt, but forget altogether how learned it, and she believes that medieval schemes education did the job rather better For the syllabus divided into two parts, the *trivium* and the *quadrivi* and the whole of the first part (the *trivium*) was with teaching the pupil how to think and how to lear how to use his tools, in fact

The *trivium* consisted of grammar, dialectic, rhetoric, in that order, which fitted themselves well, she says, to three stages of childhood—the "p parrot," the "pert," and the "poetic" G meant learning (at an age when glib learning is easy) structure of a language—usually Latin—and later to use language: how to define terms and make accurate statements, how to construct an argument and detect fallacies, one's own and other people's Dialectic embraced logic and disputation—both well suited to the pert age in which the young are fond of contradicting, answering back, and catching other people out Since the nuisance value at this age is in any case high we may as well canalise this natural argumentativeness she thinks, *by teaching children to argue rationally* accurately, and persuasively, and at last to defend a thesis publicly against critical opponents Graduating from this to the age of rhetoric—the poetic age—the pupil had thrown open to him the world's store of knowledge and with the tools of learning now at his disposal he could pursue his studies appreciatively and critically, fitting himself for the *quadrivium* the university course

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[1] *Universities Quarterly*, May, 1953, p 298

[2] London Methuen. 1948 Pp 30 1s

There is room in such a scheme Miss Sayers points out, for a liberal education for the mind needs to be exercised on other things besides Latin grammar—on verse and prose myth and legend, history, geography natural science mathematics, and theology ' It is in the highest degree improbable, ' she admits at the outset of her paper " that the reforms I propose will ever be carried into effect." Yet she persuades us to pause and consider how valuable such an education would be for those coming up to the university to study medicine. They would take to scientific method like mercury to metal; they would be able to define terms, to detect fallacies to express themselves ably and unselfconsciously to argue rationally, to write at least one language well and to light their own field with some glimmerings from the world's literature. These are benefits we cannot hope to see in our time; but it is surely possible to find opportunities, in the medical curriculum to give our students some sense of cosmos, some realisation that medicine is a small province in a universe of learning

OPERATIONS ON THE AGED

THE proportion of old people among the population of civilised countries has been increasing for fifty years and, unless some unforeseen factor intervenes, it is likely to go on increasing in the immediate future The surgeon must therefore deal with an increasing number of patients in the older group and it is important to determine whether an operation on them carries increased risks and, if so, what precautions should be taken to avoid these risks.

The question is well discussed in a recent paper by Cole.[1] Basing his conclusions on a consideration of 656 operations performed at the Illinois Research Hospital Chicago from 1948 to 1952, he gives a very hopeful outlook for those over the age of sixty who have to undergo operation There were 2557 patients under sixty, and 1090 over that age The mortality rate for major operations was 2 07% in the younger group compared with 2 95% *in those over 60* There was no significant difference between the groups for the operations of radical mastectomy, cholecystectomy colectomy gastrectomy herniorrhaphy and thyroidectomy but the older group did not do so well after œsophagectomy pneumonectomy excision of the rectum and radical operations on the mouth and neck.

The results achieved by Cole and his colleagues are astonishingly good for the figures given by other surgeons are by no means so encouraging but every surgeon will agree that the prospect of success in operations upon old people is today very much improved by the greater care taken before and after operation, the better methods of anæsthesia, and the advances in operative technique and in combating infection Perhaps full advantage is still not being taken of these benefits Flemming[2] has found that fractures in the old are still treated less thoroughly than they should be, and that thus the patient may suffer avoidable disability and a hospital bed may be occupied needlessly long

Older people differ greatly in their reactions to operation A man is as old as his arteries they say, and the elasticity of the arteries diminishes at a varying rate in different people but, generally speaking the surgeon can operate on older people with comparative safety if certain precautions are taken Any anæmia or an inadequate blood volume must be corrected and hormonal deficiency made good The blood protein and non protein nitrogen should be determined, and the serum levels of sodium potassium, and chloride estimated and any imbalance corrected Before operations on the biliary tract the hepatic function should be examined and in patients with heart-disease it is important to know the cardiac reserve Cole states that in some instances a very bad general condition can be much improved by giving 100 mg of corticotrophin (A C T H) daily for five days before operation. His wise advice is that ' the surgeon should be prepared to choose a shorter procedure, or perhaps adopt a stage procedure if the patient's condition should deteriorate significantly during the operation. '

With modern methods of anæsthesia postoperative chest troubles are rare but in the aged deep breathing exercises are a particularly valuable guard against pulmonary collapse and aspiration of the bronchi by tube-suction or bronchoscopy must be performed at once if collapse does occur Early ambulation may prevent thrombosis but in feeble patients this may be impossible After all one must make some concession to age

SAFE CUSTODY

CUSTODY is a word which has got into bad company It began kindly enough by meaning safe keeping protection ' "charge,' care,' guardianship That was in 1491, but in the early 17th century it started to form associations with confinement, imprisonment,' and durance. Even nowadays, when we use the term, we think more about the safe keeping of society than of the person taken into custodial care—who may be a sick person or a child

In an erudite study of the word and its influence on practice, Dr John R Beith Robb[1] physician superintendent at Woodilee Mental Hospital Lenzie Glasgow argues for a scientific understanding of the custodial relationship in order to place that relationship on a more civilised level He gives examples from Scotland in the 18th century, showing how failure to define the word custody, and its abuse, left prisoners with no redress for inhuman treatment The word in its crude sense has been carried over to other closed communities—he cites the old Bridewells, workhouses and recent concentration camps For the purpose of his analysis of the degradation found in these closed communities he defines custody as *that relationship which arises* when one person the Custodian gains power over another person animal or thing irrespective of purpose and with or without legal authority Since such a relationship can become depraved, reformers have continually demanded that it should be regulated by statute Legal enactments, however use the terms safe custody strict custody ' and place of safe custody without clear definition of these words The interpretation that ' safe custody means safe *from* escape is that of the 18th-century gaolers This interpretation Dr Robb whole heartedly rejects claiming that safe should mean safe from the risks of degradation "

Having classified public laws, over a period of 2000 years according to risk, he finds that legislators have been endeavouring to contend with five types of risk—namely vice, ignorance, disease, violence, and property risks Dr Robb holds that these risks are not only inseparable but are all transmissible to the society in which the individual affected—whether as victim or aggressor—is transferred This constellation of risks he describes as "degradation" Perpetrators and victims of risks have at all times been removed from the community at large and placed in closed communities, the risks travelling with them Institutions which have no proper facilities to prevent the spread of the risks imported into them become slum institutions and unfortunately this type of institution is quite common throughout the world

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[1] Cole, W H *Ann. Surg* 1953 138 145

[2] Flemming C. *Lancet* 1951 i, 758

[1] *Surgo* (Glasgow University Medical Journal) 1953 19 121

In a State service, where great numbers of administrators and employees have been given authority over greater numbers of persons in public institutions, a group custodial relationship arises Yet it is not clear who are the persons responsible for the safe custody of people in public institutions If, on occasion, the obligation of trust fails, the tendency is to name some official as responsible, even though that official may have no executive powers Dr Robb contends that an anti-degradation philosophy must be accepted at the highest official levels before it can permeate to subordinate staffs, because the physical means of guardianship are ultimately controlled at the higher levels An anti-degradation policy demands that institutions should be constructed to facilitate the work which must be carried out in them Architects in the past have designed and erected the most unmanageable of buildings, many of which are still occupied In such badly designed places, there may be provision for medical treatment and an abundance of kindness, and yet custody may be far from safe We share warmly his opinion that the architects and also the servicing departments should thoroughly understand the anti-degradation philosophy

Dr Robb concludes that where the words "safe custody" appear in an enactment dealing with a public institution, the interpretation of "safe" should mean "safe from the risks producing degradation" He warns that "strict custody" always tends to be dangerous, so all who are directly or indirectly responsible for the custodial relationship are under an obligation to cooperate for safety Public institutions might then approximate to that state which the law styles as "places of safe custody" irrespective of the specific purpose of the institution

FIRST STEPS IN EMBRYOLOGY

WE shall probably never be exactly certain of what takes place in the darkness of the human fallopian tube when the ovum is fertilised, but the last few years have seen a steady accumulation of indirect information which enables us to make a reasonable guess Circumstantial evidence is here, as often in the law court, almost as valuable as an eye witness account The latest weapon to be turned on this fundamental target is the phase-contrast microscope By its use, Odor and Blandau[1] studied the changes in living rat eggs removed from the fallopian tube, and the behaviour of spermatozoa in relation to them Now Shettles[2] has applied this technique to human ova removed at operation either from the ovarian follicle or from the tube, and he has taken some remarkable photographs The ova were exposed to semen in vitro and incubated at 37°C for varying periods Shettles finds that the corona and cumulus cells are rapidly stripped off a follicular ovum when small pieces of homologous tubal mucosa are added to the preparation, this stripping is not effected by hyaluronidase or by semen alone He failed to observe any evidence of a specific attraction of the ovum for the spermatozoa, though those which come in contact with it by chance become fixed to it In vitro the ovum can apparently be penetrated by several spermatozoa, though whether this occurs in vivo is uncertain. It also appears that the whole spermatozoon may remain intact after penetration of the ooplasm, as has been reported in several mammals

Such studies, carried on under artificial conditions merely indicate probabilities, but they confirm that human as well as mammalian ova can be used to give information about the process of conception The e work of Hamilton[3] in this country and Rock and his colleagues[4,5] in the U S.A is thus being extended, and phase contrast microscopy has now proved its value investigations of this kind

RECURRENT PAROTITIS IN CHILDHOOD

THE pioneer work of Payne[6] in the '30s added much to our knowledge of recurrent parotitis, but this disorder, which is by no means rare, continues to pass unrecognised Published accounts of it are few, the largest series of cases in children was published in the States by Bigler[7] a few years ago Attention has been drawn to it by Everley Jones,[8] who describes cases in children observed over a period of five years the Midlands

Recurrent parotitis shows no decided age distribution though it is probably commoner in adults than children In children it seems to be equally co in each sex, but among adults it is much commoner women than in men The principal clinical feature swelling of one or both parotid glands, recurring one more times The whole gland enlarges and is usually tender, and when recurrences are frequent some enlargement may persist between exacerbations The frequency of recurrence may vary from weekly to yearly In the active phases there is always some discomfort, and usual pain which may be severe In most cases the orifice Stensen's duct usually looks normal, but in very acute episodes redness and swelling may be seen around Turbid saliva can nearly always be expressed, while severe cases purulent saliva can occasionally be seen drip from the duct orifice In most cases the secretion produces the "snowstorm" effect described by Pa, this is caused by small accretions of cells and mucous casts of ducts, suspended in turbid saliva Calculi not formed The diagnosis is confirmed by sialog This valuable investigation, developed by Payne, r characteristic changes which Everley Jones found in of the 14 children in whom it was done When sial graphs are taken after injection through a blunt nee of 1–2 ml of a radio-opaque fluid into Stensen's spherical dilatations of the finer ducts are displ, occasionally dilatations, usually fusiform, are seen in the main ducts The dilatations are sometimes mental There may be no fever, and the white blood-count is usually only slightly increased Payne ob that patients with recurrent parotitis are in g constitutionally nervous, and he suggested that instability of control of salivation via the cranial autonomic sys might be a causal factor

As in other series, Everley Jones isolated α haemoly streptococcus (*Streptococcus viridans*) from the ma, of his cases, this organism was found alone in 12 and association with a pneumococcus in 3, while a pneu coccus alone was isolated in 2 The pneumococcal which seem to be relatively commoner in children th in adults, are usually more severe than the streptoc and suppuration may occur, but rupture through parotid fascia is rare Pathologically the disorder mild chronic sialodochitis with recurrent exacerbations which lead to attacks of subacute parotitis

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[1] Odor D. L Blandau, R. J. *Amer J Anat* 1951 89, 29

[2] L B *Amer J Obstet Gynec* 1953, 66 235

[3] Hamilton W J *J Anat Lond* 1944, 78 1, *Ibid*, 80 224

[4] Rock J Hertig A H *Amer J Obstet Gynec* 1948, 55

[5] Menkin M F Rock J *Ibid*, p 440

[6] Payne R T *Brit J Surg* 1931 19 142, *Lancet* 1933, i, *Proc R Soc Med.* 1938, 31, 398 *Brit. med. J* 1940, i,

[7] Bigler J A. *Med Clin N Amer* 1946 30 97

[8] Jones H E *Arch Dis Childh* 1953 28, 182

It may seem strange that this disease rarely affects the other salivary glands. In Payne's series of 52 cases of recurrent sialadenitis the parotid glands were affected in 50 cases and the submaxillary glands in only 2 Dissimilarity in structure and function are thought to be the *reasons for this selectivity the parotid glands are* entirely composed of serous acini drained by long narrow ducts—even Stensen's duct is narrow—whereas the mixed serous and mucous acini composing the submaxillary and sublingual glands are drained by wider ducts Infection of the parotid glands is undoubtedly facilitated by the greater tendency to stagnation of the secretion and the presence of only a small amount of bactericidal mucus in the secretion A source of infection in the mouth nose or throat such as carious teeth or septic tonsils, is found in a significant proportion of cases There is no doubt that almost all forms of acute and subacute parotitis are caused by ascending infection Bruce Pearson[9] described 11 cases of recurrent parotid swelling in children in which there was no evidence of infection but usually there was a history of allergy and he believed that allergic swelling causing obstruction of the duct produced the parotid enlargement

Recurrent parotitis is usually regarded at first as mumps but once there have been several relapses the diagnosis becomes clearer Acute staphylococcal parotitis, which soon gives rise to pus and is not recurrent, and neoplasm sialolithiasis, and sarcoidosis which have distinctive features and are rare in childhood are unlikely to be confused with recurrent parotitis. Treatment should consist in eliminating septic foci in the mouth nose and throat—notably carious teeth and infected tonsils All workers agree about the importance of massaging the gland towards the duct orifice, to counteract the tendency to stagnation of secretion which increases with infection Massage should be done before and after each meal and also in the morning and at night. Instillation into Stensen's duct of penicillin or other antibiotic to which the infecting organism is sensitive is usually helpful though it does not as a rule bring about immediate cure Assessment of results is difficult because spontaneous recovery is possible; but in Payne's series before the introduction of antibiotics the average duration of the disease was nine years.

THE TELL-TALE HEART

READERS of Poe will remember the murderer who buried the corpse under the floor but was undone by his victim's heart, which obstinately refused to stop beating and moreover did so with such loudness that it drove the unhappy slayer to madness and confession Such an audible manifestation of cardiac activity is rare even in life and this is perhaps fortunate for otherwise systolic pinking due to low protein octane-rating might well have become part of modern advertising mythology *Occasionally however disease of the heart* or lungs may produce sounds which can be heard with the unaided ear at distances from a few inches to several yards away Bean,[10] of Iowa, has lately collected from his own and from published records 164 instances of this unusual and interesting phenomenon In about one third of the cases described the audible sounds were in fact very loud valvular murmurs usually produced by free aortic regurgitation These are variously described as 'croaking' 'humming' 'whistling' or cooing or some other musical term Pneumothorax or interstitial pulmonary emphysema, either traumatic or spontaneous account for another third and in such an event the sound is usually said to be clicking crackling or "bubbling Pneumopericardium is a less common cause of similar noises. A loud "mill wheel' murmur may be produced by the churning of blood and froth in the right ventricle after air-embolism Hiatus hernia sometimes seems to act as a sounding board for the heart and occasionally a normal stomach distended with air and fluid may do the same thing Very rarely audible heart sounds without apparent cause have been recorded

Loud heart sounds are usually not in themselves of great consequence but they may be alarming and disturbing to the patient Anxiety can usually be dispelled but the disturbance of sleep may be troublesome Bean tells a sad story of an unusual affair of the heart a young man was banished by his wife to the spare bedroom because his heart kept her awake but fortunately the disturbance proved transitory

EPILEPSY OF LATE ONSET

THE onset of fits in middle and late life always raises a diagnostic problem Since epilepsy is a symptom quite as much as a disease sui generis there is always the possibility of some underlying progressive cerebral lesion even when there is evidence to suggest a constitutional predisposition The view that a progressive brain lesion in particular a neoplasm is responsible for the majority of fits coming on in middle age is still widely expressed in medical textbooks and Penfield[1] seems to give it his support But there is now evidence against it Nattrass[2] followed up a group of patients whose fits started at 40 or later and he found no evidence of progressive brain disease in the majority of them Berlin[3] supports this finding by his series of 125 men whose grand mal seizures started at the age of 35 or later 59 cases were followed for less than three years 30 for three to seven years 21 for eight to fifteen years and 15 for sixteen to twenty five years No evidence of general or neurological disease to account for the seizures was found in 84 patients, while in 40 others severe closed head injuries cardiovascular disease, or alcoholism were considered to be at least partly responsible Indeed many neurologists would agree that the grand mal seizure at any age without focal aura or focal onset, is more likely than not to belong to the group where no local lesion can be found

The question remains how far in a given case we should pursue the search for a possible progressive brain lesion which may be accessible to surgical treatment Most physicians would be content with the findings of a thorough neurological examination, an X ray examination of the skull and a carefully planned electroencephalogram in the elderly patient, with evidence of vascular changes, who had a few isolated fits If fits increase, however or the patient is rather younger and there is nothing to suggest vascular change the question of examination of the cerebrospinal fluid (C.S.F) and air encephalography or angiography will sooner or later arise If the C.S.F is abnormal then encephalography should be done unless there are special reasons against this *investigation, such as the general condition of the* patient or evidence of raised intracranial pressure Further if the fits are focal in onset or have a focal aura then carotid angiography on the appropriate side should be undertaken: for focal fits in the middle aged usually indicate a local, though not necessarily progressive lesion Their significance is quite different in infancy or early childhood when a focal onset to convulsions of any sort is far more common When the C.S.F is normal the value of intracranial air studies is doubtful Marshall and Whitty[4] for instance, found that in 52 Service patients, who had their first fit between 20 and 40 years of age and who showed no abnormal neurological signs, air encephalography was of no further diagnostic value Berlin's findings are similar of 57 patients on whom air studies were performed, only 1 showed a localised abnormality—a traumatic cyst, known to be of some years' standing—and only 4 others showed significant generalised ventricular dilatation Moreover, in reviewing another group of 81 proven cases of supratentorial brain tumour, he found that 3 had normal air pictures one year after the onset of epilepsy, and another 1 four years after the onset

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[9] Pearson, R. S. B *Ibid* 1935 10 363
[10] Bean, W B *J Amer med. Ass* 1953 152 1 93

[1] Penfield, W , Erickson, F C Epilepsy and Cerebral Localization London 1941.
[2] Nattrass, F J *Brit med. J* 1949 i, 43.
[3] Berlin, L. *J Amer med. Ass* 1953 152 794
[4] Marshall, J., Whitty C. W M. *Brit. med. J* 1952 i 547

The facts certainly cast doubt on the value of this investigation in grand mal epilepsy without focal signs On the other hand, the diagnostic value of focal fits or the presence of focal signs is well illustrated, for in Berlin's series of subsequently proven brain tumours presenting with epilepsy, 59% had jacksonian attacks, and in 85% either jacksonian attacks or neurological signs of a focal lesion developed within a year of their initi l fit These figures support the growing impression amongst neurologists that epilepsy of late onset may still be of "idiopathic" type with a relatively good prognosis This does not relieve us of the necessity of investigating such cases fully, because the occasional slow-growing neoplasm, which does present in this way, may be readily and successfully treated Negative findings from a full investigation enable the clinician to give a reassuring prognosis with added confidence, and continuing freedom from a focal element in the pattern of the seizures, and from neurological signs, suggests that this confidence has been justified

NEW OPTICAL AIDS

MANY of the partially sighted can read comfortably if the type is large enough The National Institute for the Blind has done much research on the use of large types, and its committee on the education of the partially sighted found that books in 18-point type—

that is, in type of this size—

could be read comfortably by most of the children tested The cost of producing enough books in this type is prohibitive, however, and the same applies to books reproduced in large type by 'Photostat' In 1946, a joint committee of the Institute and the London County Council was appointed to advise on the use of optical aids for this group of handicapped people, and has now reported[1] The committee concentrated on magnification by lenses or projection, and on handwriting When part of a page of type is seen with both eyes through a lens, two monocular images, which do not coincide, are formed One of them is farther from the lens than the other, and displaced to one side of it Moreover the distance separating the two images varies as the sight sweeps across the lens from one side to the other The eyes have thus to make constantly changing efforts at accommodation and convergence, in the attempt to fuse the two images into one In some people this causes headache and eye strain, but the committee says this is not necessarily harmful It was decided, however, to experiment with lenses of greater magnification and a wider field of vision than any on the market With the coöperation of the research department of Imperial Chemical Industries Ltd, two aspheric plastic lenses were produced, one $4^1/_2$ in in diameter, the other 6 in, and both having a magnification of 3 with focal lengths of 6 in The magnification was satisfactory but the distortion and chromatic aberration could not be quite overcome with lenses of this type Nevertheless plastic lenses—once the mould has been made—can be produced very cheaply, though they are, however, easily scratched They can easily be protected by two sheets of plain glass, but these introduce annoying reflections In the earlier models, electric lamps were fitted along the stand, so as to shine on the page, and coloured fil were often used to cut down glare, for this amber seemed to be the most satisfactory colour fluorescent lighting was introduced, however, these reading lights proved unnecessary, since it was pos to get good illumination throughout the school they carried, in any case, the inconvenience that had to be fitted to every desk

The aim of the committee was to examine capable of covering the whole width, and half the of a page of an average size book, and they studied lenses in particular

The 'Lenslite' (glass), 8 in focal length, plano-magnification 2 5

The 'London' or 'E D L.' (glass), 11 in focal length, bicon magnification 1 9

The 'Britex' (plastic), 10 in focal length, asph magnification 2

These were tried in schools for the partially sighted, it was found that the children liked the 'London' the 'Britex' about equally, and better than the lite' These were children whose visual acuity ra from $^3/_{60}$ to $^6/_{18}$, though most of them had less than They were also tried with binocular loupes, consistin a pair of spherical lenses worn as spectacles over ordinary correction spectacles, with the bridge of loupes resting on the lower part of the nose The pa lenses forming these loupes are as though taken from edge of a single large lens, and as a result there is a optical centre, and the reader does not have to make effort to converge the eyes to look at a page held at focal length of the lens combination (The magnific is about 2) Loupes of course, can be carried about easily than lenses mounted on a reading stand, and draw less attention to the user The children, how did not show any particular preference for the over the mounted lenses

Magnification by projection can be achieved either enlarging the projected print by means of lenses, with without mirrors, or by microphotography of pri reading matter, which is then projected on to a The first is done by the various types of episcope (w project on to a screen at a distance from the appara and also by other devices which, by a system of project the print on to a ground glass screen conta in the apparatus itself The magnification, with types of apparatus, can be varied—with the episcope varying the distance of the projector from the and in the combined units by the choice and positio of lenses Any printed book can be read with these of apparatus, but the contrast between the print background is poor, and the machines are expen Moreover, it is hard to get the pages of the book flat there is some distortion, and every time a page is tur the book has to be adjusted so as to bring the first into the correct position for reading Print can also photographed on to a microfilm and projected on screen, this device has been developed in America patients obliged to lie flat in bed the print is pro on to the ceiling, and a simple switch panel, managed the patient controls the movements of the film films are 100 ft long and carry 1600 pages, which from right to left[2] An apparatus of this type was insta last year at the Miller General Hospital, Greenwich[3] joint committee is conducting experiments to assess value of these microfilm projectors for individual, for class, use

Coloured "blackboards," and different-coloured have been used in some schools to help partially sig children to read handwriting easily The children in school prefer blue chalk on a yellow board, but vary

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[1] The Use of Optical Aids for the Partially Sighted N I B, Bulletins no 19 The National Institute for the Blind 224, Great Portland Street, London W 1 1953 Pp 16

[2] See *Lancet*, 1945, ii 31

[3] *Ibid* 1952 ii, 943

Public Health

AN INFECTIOUS DISEASE INTELLIGENCE SERVICE

A W S THOMPSON
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IN a country like New Zealand where the local health departments administer the social security medical scheme contacts between general practitioners and the medical officer of health are liable to be of a somewhat unpleasant kind In my own district which covers some 000 sq miles and has a population approaching 450 000, there are over 400 doctors in private practice, and it is impossible for the M O H to know more than a few of them well In such circumstances the doctor's most frequent reminder of the existence of the health department is apt to be an inquiry about his claims for payment from the Social Security Fund As a result he comes to regard the M O H as a snooper and checker of forms rather than as a colleague who happens to be a whole time officer of the social medicine services Two years ago I began an experiment in coöperation between general practice and public health and this has been so successful as to seem worth describing

An Experiment in Coöperation

I began by getting in touch with 10 general practitioners scattered about the city area of Auckland. I explained to each that I had felt for a long time that my department was not sufficiently in touch with the work, thoughts, and opinions of the general practitioner At the same time we had no means of collecting accurate information about the prevalence of non notifiable diseases such as measles whooping-cough diarrhœa, and vomiting I invited the doctor to become a member of an unofficial group of practitioners who would send me each week a voluntary return of the numbers of new cases of certain diseases seen in the past seven days with comments on other illnesses prevalent among their patients On my side I would let them have each month an analysis of the returns from the group with any other useful information about illness in the city which came my way from other sources I also suggested that we might meet together once or twice a year to review our work and discuss matters affecting general practice and the health department.

Rather to my surprise I met with no rebuffs. Every doctor I approached agreed to join, and none of them thought that the preparation of a weekly return would be very difficult or too much trouble

The first meeting of what we now call the Medical Practitioner Group was held on Nov 31 1951 After talking over the plan for setting up an infectious disease intelligence service we had a general discussion about illnesses prevalent in Auckland at that time. We went on to consider some health department activities in which the general practitioner was interested. These talks were so stimulating that it was decided to meet again the following month and we have been meeting once a month ever since At the second meeting I thought it wise to point out that I had not formed the group as an advisory body to guide the policy of the local health office. I was anxious to obtain through the group opinions on various matters concerning the health department and general practice and would carefully consider them but I did not undertake to accept its guidance where they conflicted with my own convictions. On this basis the group has functioned very happily

WEEKLY REPORTS

The practitioner makes his weekly report on a cyclostyled sheet with the following sections:

1 Total number of *new* cases seen in last seven days
   Chickenpox
   Mumps
   Measles
   German measles
   Bornholm disease
   Acute laryngo tracheitis
   Whooping-cough
   Infective hepatitis
   Diarrhœa and/or vomiting
   Influenza
   Otitis media
2 Notes on D and V cases *Impressions* of age-groups mainly affected type severity &c.
3 Note on types of influenza.
4 Other prevalent illnesses and remarks

Two further items were added later because of current *developments in the city*

Infective hepatitis.—Please give name and address of any case of jaundice with history of blood or plasma transfusion in past 18 months

Acute nephritis —Please list any definite cases, whether sent to hospital or not.

Herpangina has now been substituted for acute nephritis in the weekly returns

Before the end of every month forms for each Friday in the next month are posted to the doctor, each having a stamped addressed envelope clipped to it. He asks his nurse to place the appropriate form in front of him every Friday afternoon, for completion from the notes which he keeps in his pocket-book If the doctor is away the form is sent in by the nurse suitably endorsed To preserve uniformity and accuracy information from locums or assistants is not asked for obviously some locums would be less enthusiastic about this than others

At the office my personal clerk checks the forms in each week and reminds the doctor's nurse by telephone if any do not arrive promptly When this happens it is usually due to an oversight; somebody has forgotten to post the envelope One member of the group was ill for the greater part of the first year, another who had to resign owing to overwork was not replaced immediately and most were off duty at some time or another but we have averaged more than 8 completed returns each week in the first twenty months. In the monthly analysis all figures are "stepped up" to show the calculated numbers of cases for the whole group of 10 doctors, so that direct comparisons can be drawn from week to week. There are 114 general practitioners in practice in the city and the group handles about a twelfth of the work of the area. Multiplying their figures by ten therefore gives a fairly reliable conservative estimate of the prevalence of diseases in the community—or at least of the cases seen by doctors

MONTHLY SUMMARY

The monthly summary includes a table of the figures for the year up to date, and a digest of the notes and comments by doctors Charts showing the prevalence of certain diseases week by week and their distribution by the areas covered by members of the group are kept in my office. In 1952 there were rather severe epidemics of influenza and mumps and as the observers are dotted more or less from west to east across the city the spread of each disease could be traced as well as its general incidence

Discussion

The value of this experiment from my point of view can hardly be overstated It is a good many years since I gained my own small experience in general practice and that was not in New Zealand Now at least I can learn by regular friendly personal contact what the practitioner is thinking and what difficulties he is meeting with

Now and then I send out a circular letter to all practitioners in the district containing information about prevalent diseases new health department facilities, and so on These letters seem to be well received From time to time information obtained through the group can usefully be sent out in this way In July last year, for instance, many cases of acute nephritis were being treated in hospital, and I learned from the group that about six patients were being looked after at home for every case sent to hospital In some children hæmaturia had been noticed for several days before advice had been sought A letter giving details and emphasising the importance of absolute rest from the onset was sent out to all doctors, and a little later warnings were published in the newspapers Civilian epidemics of acute nephritis are rare, and even in this considerable outbreak most doctors saw only a few cases Several doctors told me later that it was only after getting this warning that they realised what was going on—one of them in the case of his own symptomless hæmaturia

Except in emergency it is best to let the profession have information of this kind in advance of the general public, but when any infectious disease is unusually prevalent I give a monthly statement to the press

The onset of a new epidemic of poliomyelitis was heralded several weeks beforehand by suggestive illnesses reported in detail by members of the group Toxic labyrinthitis, otitis media, and a vesicular pharyngitis, which may be related to the "herpangina" of the Coxsackie virus, have been shown to be remarkably prevalent Bornholm disease and infective hepatitis are being watched Acute laryngo tracheitis, a fairly recent immigrant, has just been added to the weekly report list It is obvious that there is plenty of material here for speculation and research

Quite often a medical officer of health gets a telephone inquiry from a newspaper office about an outbreak of measles, mumps, influenza, or some other non notifiable condition How humiliating it is to have to explain one's ignorance of the situation ! With this scheme in operation it is very different We not only know what is going on, and can hazard estimates of the distribution and extent of any outbreak, but if there is any unusual illness in the community we have a means of getting reliable information at very short notice

Our records should also be useful in time to come if it is desired to ascertain, for example, the influence of the minor epidemic diseases on pregnancy With some diseases, such as rubella, this method of estimating prevalence is probably more accurate than statutory notification, which is notoriously unreliable for diseases not treated in hospital

The enthusiasm of the group seems to grow from month to month, but membership has been limited to 10, not only because that number makes it easier to circulate information and maintain personal contact, but because enthusiasm too widely diffused loses its virtue As time goes on members will be lost for one reason or another, and replacements of equal energy and spirit may not be forthcoming But already the experiment has shown that one kind of cooperation between general practice and the health department which I had not thought possible under present conditions can in fact be achieved

The formation of a discussion group was not a definite part of the original plan, and I do not know how it will eventually work out We meet at 8 30 P M (nearly all New Zealand doctors have an evening surgery) and we made it a rule that meetings would close at 10 30 P M , but discussions generally end on the pavement We have no fixed plan, so far we have met often because we wanted to get on with the subjects we were studying, and that may or may not continue We have already published two articles (" Social Security and the Family Doctor" and " Financial Aspects of City General Practice Today ")[1] and a third is in preparation

For me these meetings are both enjoyable and stimulating, and I have been surprised and gratified that men who work so hard are willing to give up so much of their time There is no better doctor than the good general practitioner, and no better man When we in the public health service find means to tap this almost untried source of inspiration and enlightenment we may at last be able to show that social medicine has a real meaning

I wish to thank Dr J Cairney, director general of health, New Zealand, for permission to publish

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Call for a Unified Service

At a meeting of the Society of Medical Officers of Health, held in London on Sept 17, Dr Andrew Toppin, the outgoing president, inducted as his successor Dr G Metcalfe Brown

In a presidential address, Dr Metcalfe Brown discussed possible developments in the public-health service and considered how the three separate divisions of the National Health Service might be modified and ultimately fused

Centralisation of government, he declared, had greatly weakened local government, with consequent reduction in efficiency and a danger of runaway national finances One suitable method of reform would be to create in the United Kingdom about fifty all-purpose local authorities, which would also be local health authorities administering the hospitals and consultant service, the general-practitioner service, and the public-health service The local authority should be composed entirely of elected members, and the medical profession and other professions should be represented by cooption to the appropriate local-authority committees, the final decision resting with the council composed entirely of elected members

Turning to the functions of the Ministry of Health, Dr Metcalfe Brown expressed regret that many of these had been dissipated For instance, the responsibility for housing, which today was the greatest public health problem, had been transferred to the Ministry of Housing and Local Government, and central control of duties relating to deprived children was exercised by the Home Office The Ministry of Health had been at its best when its duties were advisory and supervisory, but not executive

" The administrative reform of local government and the absorption by large local authorities of the present functions of regional boards, boards of governors, and executive councils would remove the large executive functions of the Ministry of Health and allow it to concentrate on its true function "

Of the hospital and consultant services Dr Metcalfe Brown said that the separation of teaching from other hospitals administratively was a mistake, and Scotland had done well to avoid this

" To base hospital administrative regions on university towns—and therefore presumably on the medical teaching schools of the universities—was as illogical and unsound as it would be if a large industrial undertaking were to base its executive administration on its apprentice training school

The administration of all hospitals by a small number of large local authorities would ensure the best use of hospitals beds, would guarantee continued clinical freedom, and would eliminate the present waste in relation to hospital administration

Dr Metcalfe Brown said that the widening of the interest of the general practitioner, and the need for preserving the continuity of medical care made a clear case for placing part of the hospital facilities under his direct control, and a unified administration would make this administratively easy

Short-term adjustments should include the return to existing local authorities of institutions for the care of the mentally defective In the tuberculosis service the local health authority, which was already responsible for domiciliary prevention, should, pending general reorganisation, take over clinical supervision in the tuberculosis clinics and the homes With regard to infectious diseases, administrative adjustments should be made to obviate the dangers of the system by which cases of infectious disease could be admitted to, and discharged from, isolation hospitals without the immlate knowledge of the medical officer of health who as responsible for prevention

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[1] Auckland Medical Practitioner Group N Z med J 1952 51 332 Ibid 1953 52 200

Touching briefly on industrial medicine Dr Metcalfe rown suggested that this should not be a separate stem, which would add to the existing disunity and igh cost of administration

> Industrial medicine is not a separate subject—it is but ne of the many applications of general medicine and public ealth. The few specialists who exist in the field of -called industrial medicine are very necessary—e g, the xpert on poisons used in industry; but surely he is a specialist toxicology not a medical officer in industrial medicine

At the meeting members rejected by 78 votes to 31 a roposal to change the name of the society to the Society f Preventive Medicine.

Poliomyelitis

A W H O expert committee which has been meeting Rome to prepare a world programme of research to the disease last weekend issued a summary of its ndings

The *Times*[1] reports that the committee recommends hat research laboratories should be set up on all ontinents under the general supervision of W H O o identify, type, and study strains of poliomyelitis irus, as well as to provide materials for diagnostic urposes in all laboratories participating

The committee declares that the virus enters the body hrough the mouth, and that the primary site of infec ion is the alimentary tract Poliomyelitis is a highly nfectious disease spread by intimate association with nfected persons."

The committee, having studied the factors predisposing to or precipitating paralysis, suggest the following precautions: (1) that operations for removal of tonsils and adenoids should be avoided during epidemics (2) that the activities of people with an illness suspected of being poliomyelitis should be restricted for a week (3) that people intimately associated with cases of poliomyelitis should take the minimum amount of exercise from 5 to 21 days after exposure, avoiding fatigue from any cause including travel

In epidemics the public are advised to take the following precautions (1) to wash the hands before eating (2) to keep flies away from all food and to wash thoroughly all uncooked food such as fruit and vegetables (3) to avoid intimate association (shaking hands, using common utensils, common towels &c) with members of a family in which a case of poliomyelitis has occurred within three weeks; (4) to treat all febrile illness with caution and (5) to avoid all over-exertion

The general movement of people into and out of communities where the disease is prevalent should be discouraged; but schools need not be closed nor public gatherings forbidden. Swimming pools with adequately chlorinated water should not be closed, but they should not be overcrowded

NOTIFICATIONS IN ENGLAND AND WALES

Poliomyelitis notifications (uncorrected) in the week ended Sept 12 (30th week of the year) were as follows paralytic 92 (123) non paralytic 81 (101); total 173 (221) This is a decrease of 51 compared with the previous week the figures for which are in parentheses This fairly sharp fall suggests that the peak of the outbreak has been passed

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[1] *Times*, Sept 21

International Conferences

NEUROLOGY

THE 5th International Neurological Congress was held n Lisbon from Sept 7 to 12, under the presidency of Prof. António Flores. The British delegates were headed by Sir Francis Walshe, F.R.S The morning sessions were devoted to discussions on four major topics while in the afternoons short papers on miscellaneous neurological subjects were presented and discussed

As was fitting in the city of Prof Egas Moniz two of the major discussions were on vascular disorders of the brain. On the first morning Dr Seymour S Ketty (Bethesda, Maryland) described the physiology of the cerebral circulation in vascular diseases of the brain Prof G Schaltenbrand (Würzburg) discussed brain pressure in relation to vascular disease Prof P C P Cloake (Birmingham) the various types of obliterative arteritis which may affect the cerebral arteries, and Dr M *Girard and Prof A. Devic (Lyons) intracranial* vascular malformations excluding aneurysms The second morning was given over to the more surgical aspects of cerebral vascular disease The discussion was opened by Professor Riechert (Freiburg im Breisgau) on the surgical treatment of thromboses; and he was followed by Professor Moniz and Dr Miller Guerra (Lisbon) on the angiographic appearances of intracranial aneurysms and angiomas Prof Norman Dott (Edinburgh) on the surgical treatment of intracranial aneurysms and Prof H Olivecrona (Stockholm) on the surgical treatment of arteriovenous aneurysms and vascular tumours of the brain.

The third major discussion was on the parietal lobes This was opened by Dr Macdonald Critchley (London) he was followed by Prof J Lhermitte (Paris) who gave perhaps the most applauded of all the contributions to the congress, on anosognosia and disturbances of the body image and Prof H Hoff (Vienna) on the coöperation between the right and left parietal lobes; while the fourth contribution by Prof D E Denny Brown (Boston) on parietal lobe apraxia was read in his absence by Dr Merritt

The last morning was occupied by papers on the metabolic diseases of the brain Prof L van Bogaert (Antwerp) and Professor Klenk (Cologne) discussed the semiology pathology and biochemistry of amaurotic idiocy Sir Russell Brain (London) described the neurological complications of Gaucher's disease Dr P Castaigne and Dr François Lhermitte (Paris) involvement of the nervous system in glycogen disease and Prof V Giampalmo (Genoa) the lipoidoses

During the congress there were a number of demonstrations the most interesting of these was a series of radiographs showing the development of cerebral angiography in the hands of Professor Moniz and Prof Almeida Lima. The International League against Epilepsy under the presidency of Dr Critchley held a discussion on temporal lobe epilepsy which was opened by Professor Gastaut, of Marseilles

Following the meetings in Lisbon many members of the congress went to Madrid to honour the memory of Ramon y Cajal in this centenary year of his birth The Cajal Museum with its interesting personal and scientific mementoes was open and a meeting was held at which tributes to Cajal were paid by Professor Ibor (Spain) Prof John Fulton (U S.A) Sir Russell Brain Professor de Wulff (Belgium) Prof. J O Trelles (Peru) and Prof F de Castro representing Cajal's pupils

HÆMATOLOGY

THE 4th congress of the European Society of Hæmatology was held in Amsterdam from Sept 8 to 12 Over 500 members were present as well as about 250 guests In all, at least 28 different countries were represented The main subjects chosen for discussion at the scientific sessions were immuno hæmatology hæmoglobin metabolism and erythropoiesis, acute leukæmia lymph node puncture the blood platelets, and coagulation Although no sensational advances were reported the congress made it very clear that hæmatology is rapidly growing in complexity and in importance as a branch of medicine and pathology In all over 100 papers were presented

There was evidence from several sources that some types of drug induced as well as idiopathic" thrombo cytopenic purpura are due to anti platelet antibodies, and that anti-leucocyte antibodies may similarly be responsible for some types of granulocytopenia Both in-vivo transfusion experiments and in vitro agglutination tests lead to this conclusion

The relation between porphobilinogen (excreted in large amounts in cases of porphyria) and the porphyrins was outlined by Prof C **Rimington** (London), it is becoming clear on both clinical and experimental grounds that barbiturates may be a potent cause of porphyrinuria Dr J **Waldenström** (Malmö) referred to a large family in North Sweden of which 150 members were known to have suffered from congenital porphyria

In the discussions on blood coagulation, the main centre of interest was the mechanism of generation of blood-thromboplastin Dr F **Koller** (Zürich) presented evidence for the existence of yet another coagulation factor ("factor 10"), and Dr N **Rosenthal** (New York) described a third variety of hæmophilia Unfortunately there seemed to be no promising therapeutic advances

Dr R G **Macfarlane** (Oxford) presented a film of marrow puncture which was particularly well received, being both educational and amusing A notable demonstration was the projection by television on to a very large screen of a series of demonstrations given in a nearby building The definition was extremely good and the demonstrations could be seen in comfort by an audience of a hundred or more

The president of the Dutch Hæmatological Society, Dr S I **de Vries**, the secretary-treasurer, Dr M C **Verloop**, and the remaining members of the organising committee deserve great credit for the organisation of this successful congress

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Points of View

PERIODIC MEDICAL OVERHAUL

Sir Adolphe Abrahams
O B E, M D Camb F R C P
CONSULTING PHYSICIAN, WESTMINSTER HOSPITAL, LONDON

Mr A B was sent to me with a tumour in the right hypochondrium so large that he himself had become aware of its presence He was a prominent executive in a large American industrial company, so valuable an employé that it was highly desirable to ensure so far as possible his immunity from illness Accordingly he had been investigated by a clinic in Detroit, and when I say investigated, nobody who has had any acquaintance with transatlantic thoroughness will need any reminder of its nature and scope For after all, what was a few dollars', or for that matter a few hundred dollars', expenditure on insurance by a wealthy company? He had been given a completely negative report only three months previously Now here was he with a retroperitoneal sarcoma, and six weeks later he was dead.

Dr C D came to me because he knew of my interest in athletics, and, proud of his physique at the age of 50, wished to exhibit himself as a remarkable specimen for his age More to please him than to entertain myself, I went through the orthodox examinations, including of course the urine To my amazement, this exhibited Bence Jones albumose I referred him at once to the experts who deal with this rare anomaly, and they confirmed my observation Dr C D succumbed to multiple myelomatosis before his 51st birthday

Sir E F consulted me for "indigestion," by which he meant vague abdominal discomfort and nausea The duration of his symptoms was three weeks, hitherto his health had been in all respects satisfactory No time was lost in appropriate investigations and within 7 days he was on the operating table Carcinoma of the stomach with widespread dissemination was revealed Presumably his lesion started *at least 6 months in advance of any symptoms*

* * *

Articles, lectures, and broadcast invocations reiterate the advantage and value of a periodic medical examination *when well* In this way, it is represented, future illness may be avoided or early evidence of trouble already present discovered and arrested Comparison is made with the routine overhaul of a motor-car—a specious but, I think, a spurious analogy To indulge in a comparison at least no less applicable, nobody, so far as I am aware, advocates regular precautionary visits to our legal advisers with the idea of protecting ourselves from misfortunes and conflicts with authority We think it more reasonable to wait until trouble arises and then to ask them to get us out of the mess

EXAMINATION

But accepting the principle, what would be the minimum examination and investigation to constitute a net fine enough to catch essentials yet coarse enough to be practicable?

Taking the temperature Examination of the cardiovascular system and the lungs Palpation of the abdomen Testing the pupil reactions and the tendon jerks Estimation of hæmoglobin, a red cell count, a total and differential leucocyte-count Testing the urine for albumin and sugar Radiography of the chest Ophthalmoscopy Sigmoidoscopy might even be included Precautionary measures might be extended to a barium meal, a barium *enema, and intravenous* pyelography, to an electrocardiogram The blood to be examined for a Wassermann reaction and for estimation of non protein nitrogen Gastric analysis, especially for achlorhydria There is literally no limit to the number of possible excursions into biochemistry

What might we reasonably expect from such a procedure? Certain superficial discoveries a lump in the breast, a polyp of the large intestine, a pigmented mole, and other potential candidates for malignancy Reassurance—admittedly on occasion with precocious confidence—is another asset Here and there entirely unexpected revelations will occur But as I have suggested, and as any practitioner will agree, only too often the most elaborate investigation fails to discover a mortal disease even in a comparatively advanced stage Against these sometimes uncertain advantages must be set the expenditure of time and money and the danger of creating hypochondriasis and what may be called disease mindedness

INTERROGATION

An alternative method of investigation is to refrain altogether from physical examination and rely upon an elaborate interrogation These are the sort of questions recommended

Have you any tightness in the chest on exercising?
Any cough? (Not forgetting, one hopes, to inquire about cigarettes)
Has there been any change in your appetite of recent date? Any soreness of the tongue?
Have you at any time seen double? Any queer sensations in your limbs?
Do you feel better in cold or hot weather?
Any bleeding from the back passage? In the case of a woman, any bleeding after coitus or since the menopause?
Have you noticed any difference in your weight?
Do you take any drugs? (Certain drugs mask symptoms or produce skin disorders or blood diseases)

It is difficult enough, and calls for considerable experience, to assess the significance of volunteered symptoms By this method the doctor would have the additional difficulty of estimating to what extent the answer is what the interrogatee believes to be genuine and what he supposes the interrogator desires

EDUCATION

It should not be forgotten that it is the well, the healthy, who, it is advised, are to be examined According to the dictionary, health is soundness of the body spiritual mental and physical well being It has been said that the conditions for health are:

- Satisfactory environment.
- Freedom from infection.
- Adequate nutrition.
- Congenial employment
- Opportunity for self-expression.
- Sufficient rest and leisure
- Realisation of a goal in life
- A satisfying home circle
- A degree of physical and mental fitness equal to possible stress.
- Ability to adapt to change

It is worth asking if it is not wrong to place the emphasis on the possibility of disease instead of on health mindedness Whatever the mechanism the will to be well is a powerful influence and an encouraging atmosphere should be created But if health routine has to be taught are doctors the best teachers? Preoccupation with disease, necessarily the heritage of our training may not provide the best milieu for health mindedness It may after all be preferable for us to come into line with our sister profession and adhere to our proper métier—the treatment of disease

Personal Papers

HOW DO I TREAT MY DOCTOR?

M A. SIEGHART
LL B

Much has been said taught, and written about the human approach of the doctor to his patient All agree that his success depends largely on the personal relationship which is established but opinions differ when it comes to deciding how this relationship should be formed—whether the principal part should be played by human kindness or perhaps by psychic intuition The truth is, I believe that the question "how do I treat my patient?" will never fully be answered until it has been countered by the far more important one 'how do I treat my doctor?'

Even the most experienced doctor requires an experienced patient one, that is to say who has studied the relationship of doctor and patient from the patient's point of view For his diagnosis the doctor must rely largely on the case-history provided by the patient. Training and practice is needed before a patient can furnish a serviceable medical history

* * *

The first data given in a case-history are usually name address, and age, and if the patient is a woman the profession of her husband For women two important points already arise First as to her age If at all possible an experienced patient will avoid giving an age between 40 and 60 for it is part of the acknowledged armoury of modern medicine to hold the climacteric responsible for all complaints arising in this period of a woman's life. The absence of specific symptoms is immaterial for the concepts of "preclimacteric" and 'post climacteric' cover precisely this contingency Every complaint from toothache to corns may be explained by ovarian deficiency and thus held to be merely functional—a consideration which delights the doctor but has never yet cured a patient.

Quite as important as the question of age is that of marital state No experienced patient will admit to being unhappily married or far worse divorced for she well knows the automatic train of thought such an admission will set in motion: a divorced woman is a misunderstood woman a misunderstood woman is an unsatisfied woman; a woman who cannot lead a full sex life will clearly suffer damage in body and soul. This chain of reasoning cannot be broken—not even by an assurance that one is leading the life of a wanton

The next point raised is the patient's family history and her (or his) constitution This leads to a thorough analysis of the lives and deaths of her ancestors Here the patient who has successfully circumnavigated the Scylla of the "functional disorder" is drawn into the Charybdis of the 'constitutional factor' The practised patient will maintain great reserve in replying to these questions: the hard boiled one will describe herself wherever possible as a foundling

Questions on birth trauma and teething can be evaded by the contention that there is no one alive who can supply this information Of the diseases of childhood the experienced patient will admit only to german measles, and that at a safely early age

* * *

If the skill of the shrewd patient has so far succeeded in depriving the doctor of the possibility of an untimely diagnosis she now has to face a far more difficult task The foundling who has successfully weathered birth trauma teething and german measles, and who is living in a state of psychic equilibrium, in the short period which separates puberty from the climacteric must indicate the symptoms that have led her to the consulting room At no point does the antithesis between doctor and patient become more evident. For the patient, the disease consists of the discomforts which she experiences in her own body To the doctor these are important only in so far as they support his diagnosis. He regards them as symptoms if he can use them and as hallucinations if they hinder him If the patient offers him nothing useful he will try to get what he needs by leading questions, and every practised patient knows how difficult it is to defend her disease against such attempts at substitution

It is still more difficult of course to decide how much the doctor should be told and even more important, in what form If the patient complains too little she is in danger of having her illness underestimated for the doctor regularly deducts at least a half from the "subjectively coloured" report of the patient as being 'one-sided' If she complains too much, on the other hand she risks a diagnosis of hysteria, hypochondria psychic disturbance, or the like—a diagnosis as fatal to the patient as it is tempting for the doctor Where the science of the human body ends, that of the soul begins. It is difficult to report a diagnosis of hysteria, for no X ray can penetrate the psyche, and even necropsy (apart from its other disadvantages) may fail to vindicate the unjustly accused

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Only the patient who circumvents this last obstacle has mastered the difficult and necessary art of correctly treating her doctor and deserves the honourable appellation of 'experienced patient.' She has recognised that the doctor contrary to the layman's belief, is not omniscient but on the contrary has at his disposal only a few well tried diagnoses. The doctor's work thus consists entirely in attempting to classify his patients under these heads. It is then the patient's difficult and responsible task to provide the clues that will guide the doctor to the right diagnosis. If the attempt fails, it must be repeated again and again but each time with a different doctor for there is nothing more hopeless than to try to change the mind of a doctor who has once reached a diagnosis.

Whoever can grasp this pattern of things and fashion her behaviour accordingly is the experienced patient struggling optimistically for health But she must recognise that she cannot demand a cure as of right. A cure can result only from the fortuitous encounter of a disease with a doctor embodying the correct diag nosis, and is thus an incredible fluke Only if she has this remarkable luck does the experienced patient become the satisfied patient, the patient *par excellence* whose medical creed runs

> " Easy it is of medicine the sense to comprehend
> " You analyse the worlds both small and large,
> " To leave it safely in the end
> " In Heaven's charge "

Special Articles

JUVENILE DELINQUENCY IN NORTH AMERICA

A NEW comparative survey[1] shows that, in the management of juvenile delinquency, the similarities between Canada, the United States of America, and Great Britain, are far greater than the main differences In Great Britain more attention is paid to due legal process, while in the U S A the philosophy of social work has exercised a powerful influence—the child's need being the paramount consideration In Canada much is owed to British concepts of legal process, but there has been a greater receptiveness to modern sociological and psychological ideas

Professor Tappan, who has made the survey, is impressed by " the widening gap between the basic philosophy of justice that has characterised court behaviour generally (in the U S A) and that which is evolving in children's courts " , and he expresses concern that courts have had virtually no attention in recent years from the legal profession and very little more from social scientists and other relevant specialists In Britain, too, lawyers as a body have neither contributed much to the evolution of an appropriate technique of administering juvenile courts, nor regarded sympathetically the efforts of others to do so

YOUNG OFFENDERS

Diversity of practice in the U S A extends throughout the field of delinquency Upper limits of juvenile court jurisdiction vary from the age of 16 to 21 years, and there is greater overlap than in Britain, between these courts and the jurisdiction of adult criminal courts Only in some 50 of the 3000 counties of the States have strictly specialised juvenile courts been established , in the mixed courts of the remaining counties the judges, without special training or experience, tend to carry over into work with juveniles the ideas and methods of adult courts Criminal courts still deal with some 20% of all children's cases—whereas in Britain today it is rare for a juvenile case to be heard in a criminal court

Professor Tappan complains that, where they exist, juvenile courts in the U S.A tend to " skirt the issue of guilt," and that there are organised efforts to convert the court into something like a general welfare agency Upwards of half the cases are dealt with informally—i e , without a charge being preferred Social investigations are made before the verdict, and often the investigation of the charge is merely perfunctory , the welfare-minded American public accept this without comment, though the practice may threaten the children's legal rights The public do not realise that the courts' capacity for providing treatment is gravely inadequate Our own magistrates are no more trained or experienced than the American ones, and a parallel can be drawn with the probation system, which, though it was introduced in 1896, is still handicapped by the poor quality of the training of its officers Professor Tappan comments " Professional social work has continued to be somewh naive about the rôle and the inherent limitations probation in a juvenile court " He makes a strong ple for cooperation between courts and child guidance clin —neither agency, he says, can function with comple effectiveness without the participation of the other

American disposal and treatment of juvenile offende are closely parallel to British , however, we learn th New York is a fair illustration of " the slow evolut towards the goals of children's court performance Even up to 1945, some children in New York we detained in jail because of lack of detention accomm dation, and in other parts of America, in 1953, this i still a commonplace Even London, that despair o social workers, is not so badly placed as that Th some juvenile court judges act on the theory that in custody is a legitimate method of correctional " shoc treatment " makes familiar reading , but the notion i spreading that to do any good detention must meet th child's mental and emotional needs and contribut towards his understanding of his position

The American penal system " outgrew," as the rep states, the use of corporal punishment by the courts the early 18th century, and the American people can congratulated on having none of the second thought the lingering longing to hit somebody—that have been much in evidence in Britain lately The list of punis ments used in detention institutions, however, mak rather gruesome reading, and includes, in some pla and to a slight degree, corporal punishment Perha 10% of delinquents are committed to institutio roughly comparable in range to approved schools borstal institutions together, and administered eith by the State or by sectarian or philanthropic as they are here These institutions, like ours, handicapped by difficulties in getting staff of calibre It follows that the training given is below standard reached in the American public schools, trade training does not get trade union recognition

British public opinion is widely convinced that battle of the Old Bailey can be won, like Waterloo, the playing fields. Professor Tappan notes this idea al in the U S A " There has been an unusual amount faith, however naïvely it, is inspired, in the value competitive athletic activities and callisthenics in development of character and self discipline " other method of treatment is used anything like so fre The ratio of psychiatrists working in State institutio to the delinquent population is only about 1 325, the complement of psychologists and social worke though rather higher in Canada, is likewise hopeles inadequate On neither side of the Atlantic has a serio attempt yet been made to develop a technique psychiatric treatment in delinquency institutions though wild and unjustified statements are made about the influence of psychiatrists in this field

PREVENTION

An indeterminate sentence is commonly used America, and makes possible a policy of release, depen ing on the adjustment of the individual Neither Br nor in the U S A is aftercare and follow-up sufficiently seriously or at a proper professional leve and the field of prevention of delinquency presents chaotic appearance Edwin J Lucas wrote in National Probation Association Yearbook, 1946

> " Perhaps the fault lies in the multitude of theories a these days concerning crime causation. Each so-cal ' preventive enterprise ' has its own concept of causation which it adheres with a tenacity which would evoke admiration if the concept were more valid Thus it has be said that crime is due to the following empty churc broken homes, poverty, parental neglect, cheap commercial recreation or not enough recreation, comics, mystery sto

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[1] Comparative Survey on Juvenile Delinquency Part 1 North America The first of a series of five regional reports planned by the United Nations Department of Social Affairs Division of Social Welfare By Dr PAUL W TAPPAN professor of [illegible]logy and lecturer in law at New York University

dio thrillers sex stimulating movies, excessive mobility of opulation illiteracy malnutrition, glandular imbalance eble-mindedness bad eyesight and infected teeth

' In pursuance of those beliefs there have been myriad hemes: the prohibition of intoxicating drinks, of coffee f some soft drinks of tobacco of juke box machines the ontrol of movies and radio the abolition of comics and elieve it or not the installation of more electric lights on reet corners. It has been proposed that parents be prose-uted and sent to prison. In San Francisco parents have been sentenced to parental schools to learn how not to ontribute to the delinquency of their children And in New ersey parents are being invited to attend classrooms with eir children.

We have also had ' boys and girls weeks and someone ecently offered a large sum of money to finance an annual crime prevention week ' Judges have placed children on robation on condition that they read certain prescribed terature and it has been proposed that piano playing is an ntidote to antisocial behaviour Meanwhile newspaper ditors district attorneys and police commissioners are onvinced that the only genuine crime preventive is the ertainty and severity of punishment, swift and punitive ustice Legislation has been passed to require the sterilisation f hopeless idiots and imbeciles and to limit immigration on e theory that the foreign born are more criminalistic than e native born.

A well known national magazine with an enormous rculation for some years has had a monthly feature devoted o techniques of crime prevention. Of the fifty two nportant men who in as many months contributed articles n the subject one was an ex president of the United States o were mayors seven were law-enforcement officials, ineteen were congressmen one was a rear admiral, sixteen ere governors five were prison wardens, and one was the dge of a civil court. There were no criminologists, sociolo ists, or psychiatrists among them

From all of the foregoing it appears that there is no end to e proposals for prevention, because there is as yet no clarity f thinking on the genesis of the phenomenon we are trying o prevent. The clarity of thinking we hope for may be npossible to achieve until behaviour scientists have licited greater exactness from the veritable mountain of onfused and confusing material accumulated each passing ecade

In Britain, too everyone thinks it legitimate to have a o at the subject of causation of crime, but any proposal o study seriously and in depth its psychological back round produces more public anxiety than support f only all speakers at political, religious, or social elfare conferences on crime could be invited to read nd helped to understand, the implications of the above uoted extract, perhaps their speeches would be shorter nd their thinking clearer

There are two interesting developments in preventive ork first the emergence, notably in New Jersey of ommunity Coördination Councils—panels of responsible ocal citizens who deal with all the delinquency problems hat can be handled outside the criminal court With olice coöperation and the support of an informed and able local public opinion this idea, competently under aken has much to commend it Secondly a Federal ct of 1040 authorises the establishment of Youth orrection Authorities—small boards of professionally ualified members with wide responsibilities for organising tate run preventive and correctional activities Being ne stage removed from judicial cares, they are in a etter position to take a wide view of the problems volved

Orthodox sociological research has revealed the ommon ecological patterning of delinquency and of ocial disorganisation in the larger cities. Social reformers ave hoped that an increased saturation of assorted elfare services in bad areas may do the trick Recently, owever, the British public too has begun to doubt hether the difficulties do not run deeper and lie in faulty elationships within the family of the delinquent. merican public opinion is nervous lest counter action might imply some inroad being made into individual freedom and some chiselling of the bases of the social order

A modern psychiatric view holds that the main hope for the prevention of delinquency and the establishment of positive mental health is in greater understanding both of intrapsychic conflict and the nature of disturbances in relationship of an individual with his family his community his ethos and his faith To gain this understanding needs deadly serious exact scientific study and to apply it successfully to delinquency requires that the legal instruments used shall be made capable of working with human nature

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MEDICAL DEFENCE UNION

At the annual meeting of the Medical Defence Union on Sept 15 Dr S Cochrane Shanks the president referred to the rising tide of litigation There are, he said several causes Perhaps the most potent is that the hospitals are now State institutions, and so are fair game In the past a patient might hesitate to sue a voluntary hospital or a doctor who gave his services free Not so today; for it is the Treasury which pays, and the doctor too now that he is salaried Another powerful encouragement to the discontented patient is the Legal Aid and Advice Act of 1949 under which litigants may receive free legal assistance in their actions against hospitals and doctors

> In this welfare social estate of ours a patient may be provided with free medical treatment by the State and may subsequently at the State's expense sue the State for negligence. He will if successful in his action, receive compensation from the State He will even if unsuccessful have his legal expenses paid by the State and, being a poor person under the Act will not be called upon to pay the legal expenses incurred by the State in rebutting his unsuccessful and sometimes frivolous suit Was even Dr Faustus submitted to greater temptation ?"

Two other factors, Dr Cochrane Shanks continued, add impetus to this flood The first is the example of the compensation paid to injured persons under the Road Traffic Act. In road traffic accidents the doctrine of *res ipsa loquitur* reigns supreme and there is in the minds of the public—and sometimes even in that of the courts—an unfortunate splash-over into medico legal cases. I have not been cured I must therefore receive compensation is becoming almost a slogan

Finally there is the attitude of the less intelligent public press Negligence real or alleged on the part of the doctor is news—maybe headline news. By the time the negligence has been disproved to the court's satisfaction the story is dead and other sensations have taken its place But the impression left with the litigious patient is obvious

The Union's council, through its representatives has continued joint negotiations with the Ministry with the object of defending unwarranted actions together and of settling just claims by a defendant in amicable agreement Dr Cochrane Shanks said that he has every hope that agreement may soon be reached between the three defence societies the British Medical Association and the Ministry

The Union's annual report shows that in the year 1952 the number of cases passed to the solicitors rose from 182 to 228 The issue of professional negligence arose in 05 cases 7 were concerned with the defence of members or the prosecution of non members before the General Medical Council 3 with unqualified practice 23 with libel and slander 42 with inquests and 26 with representation of members before one or other of the disciplinary bodies under the National Health Service In 15 instances members sought help in difficulties arising out of appointments held by them

In England Now

A Running Commentary by Peripatetic Correspondents

It was too wet to harvest, so the farmer decided to drench his sheep and lambs as a prophylactic against worms in general and liver-fluke in particular I acted as nurse, pouring out 10 ml doses into a graduated bottle while he forced the medicine—carbon tetrachloride, suitably flavoured—down their throats We watched anxiously for any of the reactions mentioned in the warning note on the tin After 48 hours, just when we thought all was well, one lamb began to stagger around in small circles, finally collapsing motionless The flock was quickly assembled with the aid of a capable sheepdog, and several of them were found to have greatly swollen ears and to be drowsy When the vet arrived he gave them all a shot of an anti-histamine compound, issued a very poor prognosis for the bad one, whom I christened Alice, and hoped none of the swollen ears would become gangrenous and fall off On our night-round all was well, but it was an anxious group that peered into the barn the next morning To our relief Alice was much better and there were no gangrenous ears—these had on the contrary all subsided On being let out to graze, however, Alice proceeded ceaselessly to beat the bounds of the field, nor did she ever stop to graze After some hours of circumambulation we put her back in the barn, where she lay motionless in the darkest corner and had to be fed on slops But when I left at the end of my holiday, Alice, after three anxious days of careful nursing, was at last beginning to perk up

The vet told us that contributory factors to the reaction were the wet weather, a recent change of diet from rough grazing to rich meadow pasture, and drenching too soon after dipping He pointed out that only lambs had been affected, and then only white-eared lambs, the pigment in black-eared lambs protecting them from the action of actinic rays Illness, it seems, is no less complicated in sheep than in humans, the dangers of drugs no less great, and after all there are hidden virtues in the black sheep of the flock

* * *

Sex and politics are the life-blood of journalism, though some papers have yet to hear of politics Slumming in the back-streets of the human marrow, the intelligent observer cannot help noting from the columns of the *Daily Blast*, the *Reticulosight*, *Kupffer's Weekly*, and the *Myeloid Courier* the interest of the average marrow inhabitant in political affairs For those who would like to dip into these periodicals a short vocabulary of politico-hæmatological terms is appended

Clot retraction	M P explaining a faux pas to the House
Shift to left	man who takes out a subscription to the *New Statesman and Nation*
Shift to right	man who cancels his subscription to *N S & N*
Red cell	shop steward
White cell	Russian waiter in Paris (see absolute count)
Neutrophil	man who reads the *Manchester Guardian*
Absolute count	man who has a whole column in *Debrett* (see white cell)
Genotype	caller for square dancing at Party conference
Genes	trousers worn for square dancing at above
Crossed genes	wrong trousers back from laundry after above
Platelet	tip for Russian waiter (see white cell)
Counting chamber	whips' smoking room
Polychromatic	man who votes for all parties
Sickle cells	Russian transfusion
Packed cell volume	number of Party members at union meeting
Tile method	slogans in public lavatories
Tube method	distributing pamphlets on the underground
Stab cell	assassin
Colour index	depth of political conviction
Standard deviation	angle of banner at Party rally

* * *

Any doctor interested in allergy could not fail to appreciate the report and photographs of a baby walrus with allergic eczema of the face due to milk in its diet Yet, such clinical findings are not unequalled in my own practice, for instance, a young woman with asthma told me that she had two canaries in her home one of whom strangely enough also suffered from asthma A miserable bird, it had been condemned to a life of wheezing dyspnœa by the veterinary surgeon Such a challenge could not go unmet, and my prescription of a 2% ephedrine solution to add to its drinking water produced a remarkable change The bird became lively and cheerful and to the joy of all it began to sing for the first time Three trials were made, with and without the ephedrine, with the same result But pleasure came with it responsibility The young woman still has attacks of asthma and is clearly feather-sensitive Close contact with feather dust is undesirable for her To which patient do I owe the greater ethical responsibility? Perhaps the decision may be made easier by the fact that the young woman cannot sing.

* * *

When I arrived in America some two years ago people said, "You're a Scotsman, aren't you?" A few months later they said, "Which part of England do you come from?" Later still, they asked, "How's Canada these days?" But I was shaken when I penetrated beyond the Mason-Dixon line and found them saying, "Y a Yankee, aren't you? How's Boston?" It will be to return home when I am hailed as a fellow citizen by someone from the East side of Brooklyn

* * *

I count myself fortunate to be a whole-time univ worker, but it means that I live modestly My hom is close to the teaching hospital, so I cannot that a car is anything but a luxury I have sold m and taken to the bicycle which I bought years ago have hardly used until now My preclinical regard me as an intellectual snob who wishes to mistaken for a proper academic worker The clinicians express concern about my health and me to a full measure of their bedside manners. students no longer bother to conceal their contempt somebody who has finally given unequivocal proof having taken the wrong path in our noble profession

But there are advantages in the new a The small amount of extra time I spend on travel is more than offset by not having a car to clean grease at the weekends On a fine Sunday, a cycle ri of twenty or thirty miles en famille gives a view of countryside not easily caught from the driving seat a hurrying car Most of all, it is easier to be an enthusiast motorist if you are not bothered with an actual machi to go wrong For a small weekly subscription y can take the *Motor* or the *Autocar* and indulge y imagination while following current trends in desi and performance One week I scream around in a Jaguar XK 120, another I move with spee distinction in a pre-war V-12 Lagonda, the last creati of the famous W O Bentley, then the stark of an Aston Martin DB 2 makes an irresistible appeal and on wet weekends I become plush-minded and along in a Rolls or Daimler You can see that as armchair motorist I now enjoy not only variety b also a class of car almost entirely reserved in real l for film-stars and gynæcologists

* * *

News from the Far East—There are about half a doz frogs jumping about my sitting room, while quite a numb are waiting outside for admission lizards of various s and in considerable numbers, 15–20 at a time, decorate walls and ceiling Useful creatures they are, since they ca troublesome insects, and I pray that there may be more them D D T resistant mosquitoes, and indeed insects every description—such as cockroaches and moths of tr mendous size—offer a paradise for the research biologist am prepared to give hospitality to anyone who wishes undertake studies with a view to getting rid of most of fellow guests I am even willing to serve as a test subj for his investigations as to whether any substance des to kill the smaller world is more harmful or less harmful human beings I can say no more

Letters to the Editor

MODIFIED BOTH RESPIRATOR

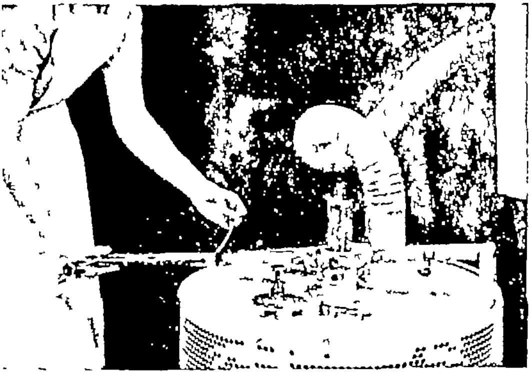
3IR,—The experience gained in modifying the Both pirator[1] and the nursing of patients in the modified pirator showed that more could be done to provide patient with greater comfort and to reduce the rsing difficulties.

ange-over to Manual Pumping

Two disadvantages remained after the pump had been odified. The first was that the change over to manual umping in the event of a failure or a cut in the electricity pply or a motor breakdown was very difficult especially ice if the failure occurred at night, the change-over ight have to be carried out in partial darkness This ight well be beyond a nurse s capabilities. The second sadvantage was that if the switch was left on the storation of the electricity supply might cause serious image to the pump unit, itting it out of action for ours and possibly days he manual pumping was so difficult and could not maintained for any length time without assistance

Dr R W Durand super tendent-in-chief at the ellington Hospital New ealand gave Captain G T nith Clarke chairman of roup 20 hospital manage ent committee details of n improved manual pump ig arrangement The credit r the basic ideas belongs to r Durand and his chief ngineer

Fig 1 shows how a nurse an change over from electric manual pumping with the ew arrangement. The com onent parts for the modified unit are included in the kit to be supplied by the Ministry of Health for the modification of Both respirators The change over consists in removing the gudgeon pin from the central shaft of the pump (a simple operation) removing the T -shaped pumping handle from its holding clips on the top of the pump unit fitting it to the horizontal pumping arm by inserting it into the tubular T ' handle and securing it with a pin attached to the handle (fig 1) Pumping can then be started and instead of having to move the handle vertically up and down as formerly, which necessitated stretching over the pump unit, the nurse can stand on the side and pumping is much easier because of the long arm of the T' handle. If the electricity is restored the pump is worked electrically and the piston going up the shaft can do no harm The nurse can then switch off the electricity for a second, reinsert the gudgeon pin through the hole from which it was removed and the electrical pumping continues when the current is switched on The noise of the pumping is much less with this new improvement



1—The "T" handle is removed from holding clips on top of the pump unit, and hen attached to the horizontal pumping arm which fits into the tubular "T handle. he handle is being secured with a pin attached to it. The hole from which the dgeon pin has been removed to allow the pumping arm to descend can be seen at he top of the shaft. The pin has been placed in the holding clips on top of the unit r safe keeping

Improved Head-board and Neck-seal

The split head board and neck seal previously described[1] was recently used for an adult male patient, and although this was much easier to use than the fixed head piece with the circular neck collar it still had the disadvantage that the upper section of the split head board when open to the full extent limited access to the patient, and the patient could not be placed prone for postural drainage The split head board has therefore been redesigned to allow the top half when opened, to slide upwards and rest on top of the cabinet.

When the bed is withdrawn there is unimpeded access to the patient and the neck is entirely free (figs 2 and 3) Moreover the patient can be placed prone for postural drainage, and a head-support has been introduced which is adjustable upwards and downwards and can be withdrawn from the head of the cabinet to allow for collection of vomit and drainage from the bronchus This has been done by making a recess in the lower half of the headpiece so that the chin is not pushed forward by the head board

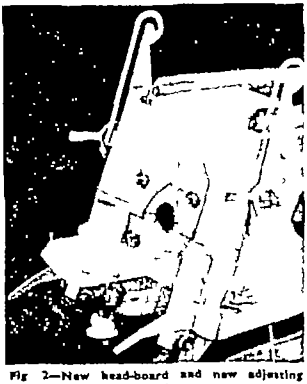


Fig 2—New head-board and new adjusting head-rest.

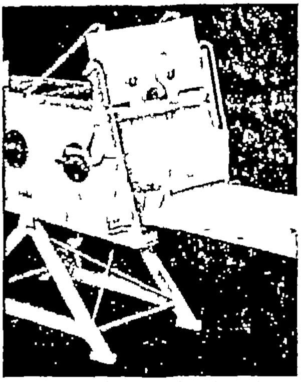


Fig 3—Bed withdrawn showing split head-board in open position.

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[1] Smith, R. E. *Lancet*, 1953 i 604

All these improvements have been designed by Captain Smith-Clarke, as were the modifications described in my earlier article, reference to which will show the difficulties of manual pumping and of getting access to the patient

Rugby R E SMITH

PREMENSTRUAL TENSION

SIR,—May I comment on your leading article of Sept 12?

In the first place premenstrual tension is not as rare as you suggest, for it was the main source of complaint in 3% of 2000 hospital patients Secondly, your suggestion that progesterone treatment is highly successful is not borne out in my experience, for though it is true that about half the cases are adequately relieved there is little result in the remainder On the contrary, most patients find ethisterone in large doses nauseating, and the common delay in the appearance of the next menstrual period is a source of anxiety to the majority of patients Inhibition of ovulation by androgen therapy during the first fortnight of the period is more uniformly successful, masculinisation is not produced by the small doses used by Bishop In any case this side effect may be completely eliminated by the use of a newer non virilising androgen such as 'Androstolone' This therapy combined with premenstrual ammonium chloride will relieve a great majority of cases

A point of considerable interest from the theoretical point of view is that these patients rarely complain of spasmodic dysmenorrhœa, and their intra uterine pressure during the flow is never high Both these facts substantiate Morton's work on the diminished progestational influence which is probably the cause of the condition

London, W 1 ALBERT DAVIS

MONILIASIS DURING ANTIBIOTIC THERAPY

SIR,—As you stated in your *annotation* of July 25, *Candida albicans* is present in the gastro intestinal tract of most normal people and, being resistant to all common antibiotics, will increase when concomitant bacteria are eliminated by antibiotic therapy

I should like to add that the elimination of bacterial competitors for food-supply is certainly not the only factor involved in this increase of *C albicans*, since it has been reported that some antibiotics have, at least in vitro, a direct or indirect stimulating effect on the growth of *C albicans*

It has been shown by Moore,[1] by Pappenfort and Schnall,[2] and more recently by Huppert et al [3] that aureomycin exerts a direct stimulation on the growth of *C albicans* in Sabouraud's broth, in Sabouraud's agar, and in a semi synthetic broth.

On the other hand, I had observed an indirect effect of penicillin on *C albicans* (1947, unpublished) When cultivated in Schopfer's entirely synthetic medium, this fungus requires biotin as the only essential growth factor When biotin is present in the medium at an optimal concentration, penicillin, even in large amounts, has no effect on the yield of *C albicans* But when biotin is added in insufficient quantity to the synthetic medium, then the presence of penicillin (about 100 units per ml) has a significant enhancing effect on the growth of *C albicans*, as if it acted in synergism with biotin When penicillin is present alone in the medium, without biotin, *C albicans* does not grow at all—a fact which eliminates the possibility of penicillin containing, as an impurity, some growth promoting factor

In the course of antibiotic therapy, elimination of some of the intestinal bacteria necessary for the synthesis of vitamins and other metabolites should have some adverse effect not only on the patient's economy but also on *C albicans* itself, which requires at least one of these metabolites, biotin However, if the phenomenon described above also takes place in vivo, the presence of aureomycin or of penicillin might, at the same time provide a way by which the fungus could overcome this deficiency and proliferate

Evidently, such observations do not yield any information as to whether *C albicans* is actually responsible for the disturbances following antibiotic therapy The abundance of *C albicans* in the stools of patients with sprue or pernicious anæmia may suggest that, in all these cases, some definite change in the metabolic environment in the gastro-intestinal tract is the common cause of the fungus's proliferation

New York State Medical Center
New York City, U S A GEORGES H WERNER

TOBACCO-SMOKING

SIR,—A leisurely investigation into the psychology of tobacco-smoking in average people, which I made over a considerable number of years, leaves me in no doubt that, contrary to what Dr H Pullar Strecker (Sept 12) maintains, tobacco is very much a drug of addiction Precisely the same fundamental psychic attitudes shown by, for example, the morphine addict to morphine are also, on close scrutiny, plainly demonstrable to a greater or lesser extent in the addict to *tobacco Certain things, however, tend to* obscure the kinship between these two addictions

The chief thing is that the textbook picture of the (for example, morphine, opium, hashish) addict, while true of addicts who have fallen into medical hands, is not a correct picture of addicts taken en masse For instance, from conversations I have had with people who have been in the East and who have had opportunities of paying particular attention to the subject it is evident that the vast majority of addicts are not miserable, depraved creatures whose one and only thought is to get hold of their daily supply nor, again, do they require increasing doses to secure the effect of the drug On the contrary, they are average, everyday people who go successfully about their everyday affairs—just like tobacco addicts in this country, provided they are assured of their 10–15 cigarettes a day

However, take away the supply of the tobacco addict and a very different picture presents itself—e g, the child who will *steal and then sell a typewriter* to get money to buy cigarettes Equivalent reactions are revealed by many adults who will spend more annually on cigarettes than would supply a much needed annual holiday, a stair carpet, or an educational endowment policy for their children's education This point can be made still more plainly by considering how, in 1952 the people of this country spent far more on tobacco (£823 million) than on the National Health Service The amount we spend on tobacco and alcoholic drink is almost a quarter of what we spend on foodstuffs Surely such figures betoken "an overpowering desire or need (compulsion) to continue taking the drug and to obtain it by any means," and justify us in concluding that the W H O distinction between drugs liable to produce addiction and habit forming drugs is "hairsplitting"

The definition to which Dr Pullar Strecker refers is unsatisfactory in that it mixes up psychological, moralistic, and social aspects, thereby unnecessarily confusing the issue I would suggest, instead, the following tentative definition of an addiction

> A psychiatric abnormality the psycho economics of which is to effect a psychic equilibrium by means of repeated dependent behaviour directed towards an external and usually inanimate object which is eventually incorporated in the body which develops tolerance to the physical effects of the incorporation on the basic psychic relations with that object being at an oral level of libidinal development and the dependence being such that equally satisfying substitute relations with *other objects cannot be established* with, consequently, the production of withdrawal ar

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[1] Moore, M. *J Lab clin Med* 1951 37, 703

[2] Pappenfort, R B Schnall E S *Arch intern Med* 1951 88 720

[3] Huppert, M., MacPherson D A., Cazin J *J Bact* 1953, 65 171

mpted substitute symptoms when the physical source of gratification is removed.

uch a definition holds even in those cases where drug is taken by injection; for in addition to the ariable oral psychic symptoms revealed on investiga 1 other psychiatric symptoms deriving from other els of libidinal development also enter into an liction and may superficially obscure the basic iical picture Such a definition also would not only 'er the 'malignant addictions, as Glover calls m but also include very interesting 'benign' lictions not mentioned in textbooks. These include 'essive milk drinking in adults (the least complicated m of addiction) and barley-chewing and turnip wing cases of which have been referred to me by ctitioners because of the chronic, compulsive, absorb , and inordinate extent of such activities

hotts, Lanarkshire. R Good

OCCUPATIONAL HEALTH SERVICE

IR,—Dr Parker, in his letter last week recognises danger of setting up a separate occupational health iical service with all the duplication and waste which t would entail So far in this country we have only ched the fringe of occupational health In the coming ırs we shall see a growing realisation that the health a man or woman must be considered in relation to his her total environment, this need applies as strongly shops offices shipyards, and farms as it does to tories An occupational health service is necessary in ler to increase both the health and the wealth of the mmunity

Such a service, however well organised at the top anot become a reality until the family doctor is enabled consider the patient in relation to all the circumstances his life. The present contribution which the 18,000 itish doctors make to occupational health is equivalent the employment of not more than 200 whole time ctors, if as many The 10% of G P.s who play some all part in industrial work must be raised to 70% or re. This can be done only if there is an efficient gional organisation for occupational health to which e G.P can look for advice and training

The Medical Practitioners Union recently published memorandum on this subject The most important nclusion reached was that an occupational health rvice must become an integral part of the National *ealth Service and not merely be coördinated with it.* is could be well achieved by transferring the Factory partment to the Ministry of Health thus keeping the perience of the Factory Department and ensuring its tegration with the other health services

The organisation of an occupational health service at gional level raises a more controversial issue Various asons (which I have no space to give) impelled us to e conclusion that the local health authority (county county borough) was the only practicable body for e purpose Each M O H would then have an additional sistant M O H in charge of occupational health The nction of the latter would be to train advise, and tegrate the work of the G.P.s in the area in so far as cupational health was concerned In the larger areas veral whole time doctors would be needed; communal udies on morbidity would be undertaken and research rk initiated

Only with some such regional organisation will G P.s enabled to play a full part in occupational health rk. No cadre of experts can replace them When I pressed this view to the T U C conference recently I s asked whether the G.P was going to learn occupa nal health at the expense of the patient. The speaker d not appreciate that sound clinical knowledge is the sis of occupational health work and that no theoretical aining can possibly fit a doctor to enter any kind of factory and deal with all its problems He *must* learn on the job

I hope that the medical profession will insist that a unified health service is the only one capable of producing true occupational health

Medical Practitioners Union
55, Russell Square
London W C.1

Bruce Cardew
General secretary

PHENYLBUTAZONE

Sir,—During the course of an investigation into the correlation of therapeutic effects with blood levels in phenylbutazone therapy we have noticed in recent months a diminution in the clinical response with a corresponding fall in the serum phenylbutazone levels, sometimes to blank values on a dose of 600 mg daily We have reason to believe this is due to a change in the coating of the tablet with consequent reduction of absorption of the drug It has been possible by splitting the tablet before ingestion to obtain therapeutic effects and serum concentrations similar to those previously obtained, without any increase in the incidence of gastric disturbance

Rheumatism Department,
West London Hospital.

Ena Bruck
M. E Fearnley
I Meanock

MALARIA IN SERVICEMEN

Sir —A number of cases of malaria have been found in Servicemen who have returned from abroad [1 2] Last year at the Military Hospital, Tidworth [3] we saw 102 cases which were diagnosed by finding *Plasmodium vivax* in the blood

Of these 102 patients, 69 were having a first attack (suppressed primary cases), and 33 had had one or more previous attacks All these patients had returned from service in Korea, Malaya, or Hong Kong While stationed overseas all patients had been on suppressive proguanil ('Paludrine') 100 mg daily which was stopped some time during the voyage home The distribution of cases was as follows

From	*Suppressed primary cases*	*Relapsed cases*	*Totals*
Korea	46	20	66
Malaya	9	13	22
Hong Kong	14	0	14
Totals	69	33	102

Clinically the patients presented with fever sometimes with a *rigor* and some with *general malaise headache* anorexia, and upper respiratory symptoms Only 34 had palpable spleens All patients responded rapidly to treatment with quinine gr 10 and pamaquin 10 mg thrice daily for 14 days Bed rest was enforced during treatment, and no serious toxic effects were noted A follow up of these cases 6 months to a year after treatment revealed 6 proven cases of relapse, and 4 in which there had been undiagnosed short-term fevers 4 patients could not be traced This accords with the usual relapse rate on such treatment

The possibility of a subclinical parasitæmia preceding clinical manifestations was investigated by blood films taken from 84 fit men of the Gloucestershire Regiment approximately 6 months after proguanil was discontinued There was only 1 *positive* result—in a man who had already had two recent attacks treated with quinine alone. Of the apparently normal men in this group 2 subsequently had attacks, one 4 days after the test and one a month later There thus appeared to be no obvious subclinical parasitæmia

The use of proguanil as a suppressive agent is now well established even though drug resistance arises in some strains of *P vivax* and *P falciparum* The latent period

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1 Macdonald, G *Lancet* 1952 ii, 45
2 Adams, A R. D., Seaton, D R. *Ibid.*
3. See MacFarlane R. G *Ibid* p 238

between discontinuation of this drug and the onset of clinical disease may be due to drug inhibition or, more likely, to the natural history of the parasite Suppressed primary malaria due to the temperate strain (from Korea) came on after an average latent period of 6 months, compared with an average of $2^1/_2$ months for the tropical (Malayan) strain The distributions of cases in men of the Gloucestershire Regiment (from Korea) and the 4th Hussars (from Malaya) were as follows

				1952				
From	*Feb*	*March*	*April*	*May*	*June*	*July*	*Aug*	*Sept*
Korea *	—	—	2	1	14	6	3	1
Malaya †	3	2	0	3	—	—	—	—

* Embarked Nov 21, 1951
† Embarked Nov 12, 1951

This attack pattern may, however, be explained on a seasonal basis, the temperate zone strain manifesting itself in the summer, and the tropical strain all the year round [4] Investigations into the attack rate in those at risk was not possible, owing to rapid dispersal by demobilisation and transfer to other units

R G MacFarlane
O A N Husain

Military Hospital,
Tidworth, Hants.

WHAT IS ULCERATIVE COLITIS?

Sir,—Mr Brooke, in his letter of Sept 12, refers to a paper by Felson and Greenberg [5] reporting that 10% of 122 patients had developed ulcerative colitis at the end of a year, following an epidemic attack of Flexner dysentery It should be added that in none of these patients had the diarrhœa cleared up since the initial attack Mr Brooke could also have referred to a later paper by Felson and Wolarsky [6] in which they give an account of 61 cases diagnosed as chronic ulcerative colitis in military personnel In 33 of these cases the onset of the diarrhœa could be traced to a definite attack of dysentery and almost all of the patients had had their initial attack where dysentery was either epidemic or endemic

I contend, however, that these patients did not develop "ulcerative colitis" in the generally accepted sense of the term Rather, their colons suffered permanent damage as a result of their attack of dysentery, giving rise to the condition best termed postdysenteric colitis This condition may have some points of similarity to ulcerative colitis and, if the destruction of the mucous membrane of the colon by the attack of dysentery is sufficiently severe, the end-result may sometimes be the pathological state of the colon, far more often seen in ulcerative colitis, described by Mr Brooke in his article [7] One would like to see the case histories of the patients who have had their colons removed by Mr Brooke, after having had bacillary or amœbic dysentery initially, but I suggest that it is possible that they had postdysenteric colitis and not ulcerative colitis, although their colons may have been pathologically similar to those he has removed from patients with the latter disease In the single example which he gives in his paper (case 4), the attack of dysentery may well have been incidental

Mr Brooke's statement that ulcerative colitis follows an attack of bacillary dysentery in a definite proportion of cases is, I maintain, based on a confusion of terminology and is not a valid argument in support of his view that ulcerative colitis is not a specific disease Let us all agree on what we mean by the term "ulcerative colitis," and if some wish to include postdysenteric colitis under this heading, let us add the prefix "idiopathic" to that great majority of cases in which the disease arises out of the blue I have already stated (July 4) some of the reasons for the belief that "idiopathic" ulcerative colitis is a disease sui generis, as Hardy put it (July 11), and I was very glad to that he, with his exceptional experience of the took so wholeheartedly this view

Worksop, Notts J M Rice Oxley

TUBERCULOSIS IN GLASGOW

Sir,—The correspondence under this heading into a general discussion on the control of tub and for this reason I may perhaps be permitted participate despite the long delay I should like support the views of Dr James,[1] who stated that was no evidence that "good housing and a good sta of living will eradicate the disease" and oppose the of Dr Paul [2] who stated that "the tubercle bacillus ubiquitous, and it is ridiculous to suggest that disease can be conquered by physical eradication of organism itself History does not give any instance the eradication of any such epidemic disease in this way

I pointed out some time ago [3] that in 1863 Budd, one of the pioneer epidemiologists, advised medical colleagues to study natural epidemics in anim in order to throw light on human epidemics the first decade of the 19th century there were pe who believed that tuberculosis in cattle could be trolled by raising "healthy" cattle with "sound membranes" that would resist tuberculosis But 1901 M'Fadyean [4] wrote

> "The man whose sense of proportion is not hope defective will attach only minor importance to such siderations, and will concentrate his efforts against the great cause of the disease—the operation of contagion. that has been successfully grappled with predispos becomes of no account "

Work on the control of bovine tuberculosis which been summarised in your columns [5] has shown at least when applied to cattle, M'Fadyean's views essentially sound, and the disease has been eradicated from Finland (where human tub still takes a heavy toll), the vast area of the U S A, the Scandinavian countries Similarly, in Great B a voluntary campaign was begun in 1935 in owners of "attested" tubercle free herds received bonuses Farmers entering the scheme were allowed sell reacting animals on the open market, and purists objected strongly to this, but the reacting were usually from the best herds, with only slight le of tuberculosis, and they entered other herds, nearly of which contained tuberculous cattle the imp thing was that more and more herds were created which there was no tuberculosis, and diseased could no longer infect the young stock Now over 4 of the 9 million cattle in Great Britain [6] are in atte herds and eradication areas have been established which reacting animals will be slaughtered All this been achieved with no dislocation of the milk supply of the trade in cattle in fact it has been achi without the great majority of people (not even, possi Dr Paul) realising that it has occurred This can perhaps be taken as an outstanding example what may be done by the old-fashioned operation enlightened self-interest (even though guided by veterinary profession) and the free play of an " market"

Cattle can obviously be handled much more than men, but there is little doubt that, despite differences, tuberculosis in cattle resembles tubercul in man as closely as any other two diseases and certa as closely as tuberculosis and diphtheria mentioned

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[4] Kehoe B L Chandler B F *Milit Surg* 1952 3 325
[5] Felson, J Greenberg, H *Amer J med Sci* 1936, 192 553
[6] lson J Wolarsky W *Science* 1947, 105, 213
B N *Lancet* 1953 1 1220

[1] James E F *Lancet*, 1953, 1, 1099
[2] Paul, H *Ibid* p 1202
[3] Francis J *Ibid*, 1949, ii, 549
[4] M'Fadyean J *J comp Path* (1901) 14, 179
[5] Francis J *Lancet*, 1950, 1, 34
[6] *Vet Rec* 1953, 65, 478

James[1] Predisposing factors must doubtless be on much more weight in human than in bovine erculosis but despite the improvement in housing and rition which had taken place by 1947[7] tuberculosis h a mortality of 55 per 100 000 was still the most portant cause of death in Great Britain Even in w Zealand, where living conditions are perhaps better n they are likely to be in Great Britain for some e, tuberculosis, with a mortality of 31 per 100 000 s the highest single cause of death in females 18–35 rs old.[6] Again in Perth Australia 55% of 1069 ldren 10–14 years old were infected with virulent ercle bacilli in 1947[8]

The assumption that living standards, particularly in gland, will continue to rise is perhaps optimistic[9] t in any event better housing and better food depend general economic development, and particularly on activities of builders and farmers There seems to plenty of room for the specific medical and sanitary asures advocated by Dr James[1] and he has already licated what they may achieve[10] one may also int out that human tubercle bacilli have been virtually dicated from the island of Bornholm[8] and there are as in the U S.A[8] where, in contrast to Australia no ool-children are infected with tubercle bacilli In smania, where there has been a vigorous campaign ce 1947 and infected persons are isolated the mortality s dropped from 42 per 100 000 to 11 per 100 000 in first part of 1953 I would submit that we must not ept the ubiquity of the tubercle bacillus it is portant to remember that all people with consumption re once ' healthy reactors,'' and as indicated by Paul[9] *the experience of war shows what will happen* these ' healthy reactors when exposed to adverse nditions.

In their delightful book *The White Plague,*[11] Dr Dubos d his wife pay a courteous tribute to the work that s been done in the control of bovine tuberculosis and rticularly the "skilful policy of segregation' that s been used in Great Britain As they say:

> ' It is by preventive measures that bovine tuberculosis s been practically wiped out in certain parts of the world, d this achievement has had far reaching consequences for control of the human disease. Wherever it has been hieved, the eradication of tuberculosis from cattle has ought about the almost complete disappearance of human fection caused by bacilli of the bovine type It has helped lower the cost of production of meat and dairy products, d has led indirectly thereby to an improvement of human trition and higher resistance to infection Moreover the t that tuberculosis has been eradicated from certain imal populations has fostered the confidence that it could o be eradicated from human populations. '

There was abundant evidence that bovine tuber losis would not have been controlled by any improve ent in the ' standard of living' and Dubos and ubos quote from my book on *Bovine Tuberculosis* hat is perhaps the most striking piece of evidence

> " In 1890 Queen *Victoria ordered* that the dairy cows on e Home Farm at Windsor be tuberculin tested Thirty five the forty cows were found to be tuberculin positive and berculous lesions were found in all of them! And yet he premises on which these cows were kept were probably e best in the kingdom and the general cleanliness left thing to be desired '

In his paper on the ætiology of tuberculosis[12] Robert och wrote:

> ' So much the *more stress* would I therefore lay on prophy tic measures, which should be directed partly towards the direct destruction of the tubercle bacilli by suitable methods of disinfection, partly to the preservation of healthy persons from contact with tubercle bacilli in all cases in which the parasites cannot be certainly destroyed.

These are the methods which have been used to eliminate bovine tubercle bacilli Obviously Koch felt that it was just as important to eliminate tubercle bacilli as it was to destroy *the organisms of cholera or* anthrax The ubiquity of the tubercle bacillus has doubtless been accepted with such complacency for so long[8] because of the difficulty of dealing with the infection now that there are chemotherapeutic agents to aid the treatment of patients and B C G to raise the resistance of exposed groups and so reduce the weight of infection there is increasing evidence that, as with cattle the rational application of hygienic methods will lead to the eventual eradication of tubercle bacilli from large sections of the population

Veterinary School
University of Queensland,
Yeerongpilly Brisbane
Australia.

JOHN FRANCIS
Professor of Preventive Medicine.

EXTERNAL CEPHALIC VERSION

SIR,—I wish to record an error in my article which I have discovered since its publication on Aug 22

It is stated that in the five year period under discussion there were 67 breech deliveries in 4217 cases—an incidence of 1 35% On re-checking this figure I find it should be 1 59% (The original figure of 1 35% was calculated on the supposition that there had been only 57 breech deliveries, but an additional 10 cases were subsequently discovered and included without a correction being made *to the percentage figure*)

The new figure of 1 59% in no way detracts from the purpose of the article—namely to justify the manœuvre of external cephalic version

If the expected incidence of breech presentation at the onset of labour is something over 3% then our corrected figure of 1 59% still indicates that by version this expected incidence can be approximately halved and *probably more than halved* as was stated in the article

Middlesex Hospital,
London W 1

M R. FELL

ANÆSTHESIA AND CARDIAC DISEASE

SIR,—Your leading article of Sept. 12 is both timely and practical, for it contains an excellent summary of the anæsthetic hazards and, at the same time, debunks some of the out-of-date views about the inevitable safety of local anæsthetic techniques.

All anæsthetists meet physicians who regard generals ' as risky and advocate locals' and even ' spinals in cases in which to the anæsthetist they would be clearly inadvisable. With the increasing knowledge of anæsthetists in spheres well beyond those of ether and chloroform—some actually understanding the significance of such mysteries as the electrocardiogram (and others like myself seeking to do so)—the nature of the help given by the physicians in bad risk cases appears to be changing Surely the opinions of the cardiologists and chest physicians are of the greatest possible value in delineating the nature and extent of the disease, the likelihood of improvement with medical treatment and any particular risk that they foresee with the anæsthetic or operation contemplated It is desirable in such cases for anæsthetists and physicians to confer rather than to leave notes such as under no circumstances should a general' be given ', ' spinal is the anæsthetic of choice here or even as one physician playfully wrote solely for my benefit, balanced anæsthesia would appear to be suitable ! Such advice is not generally sought by anæsthetists, and when given might possibly invoke the reply ' You do it yourself and you explain to the coroner '

Paul, H *Lancet*, 1932 i, 1316
McDougall J B Tuberculosis: A Global Study in Social Pathology Edinburgh 1949
Le Gros Clark, F *Nature Lond* 1953 172 4
James E. F *Lancet* 1953 i, 1252
Dubos R. Dubos, J The White Plague: Tuberculosis, Man and Society London, 1953
Koch, R The Etiology of Tuberculosis New Sydenham Society 1886 p 67

No! Anæsthesia has obtained a place as a full specialty and we are at least expected to choose wisely our technique, especially when we are aided by the physicians to a full understanding of the significance of the clinical condition

Lastly, with bigger and better surgery on older and poorer risks it seems necessary to reassert that the surgery as well as the anæsthetic causes some strain even on the heart

London E 11 E K GARDNER

PREVENTION OF POLIOMYELITIS

SIR,—The correspondence on the above subject is of considerable interest, especially to those who, like myself, have to consider how best the public may be protected

I had an outbreak of poliomyelitis in October, 1952, and ascertainment of contacts was proved most valuable by the fact that, with a few exceptions, it was these contacts who either contracted the disease or spread it as healthy carriers The latter point was conclusively proved by the virus being found in the fæces I think it is essential that child contacts should be excluded from school for three weeks, the parents are advised what to look for As regards adults only those engaged in handling children as school teachers or nursery attendants, or in handling food—for example, as waitresses or workers in food premises—need be excluded from work Incidentally if they are *not* excluded the M O H hears about it from the nervous public

The 1950 outbreak of poliomyelitis in the Isle of Wight showed clearly, according to Dr Agerholm (Aug 8), how several cases might have been prevented if adequate control of contacts had been undertaken It is incumbent on M O H s to take all steps possible to protect the public from attack by this disease, and one such step is exclusion of certain contacts

Guildford, Surrey F A BELAM
Medical officer of health

ATTACK ON FLIES

SIR,—I was interested by the annotation on this subject in your issue of Aug 8 While I appreciate your review of the ecology of flies, I think that a most unfortunate impression might be gained from the second part of the article—that regarding the possible over-emphasis on the rôle of flies as vectors of infectious disease

Two important articles[1 2] have demonstrated quite clearly the importance of flies in the transmission of dysenteric diseases These studies show that as a result of effective fly control, both in an area of high morbidity from diarrhœal disease and in one of moderate morbidity, the prevalence of shigella infections, as well as to a lesser extent of salmonella infections, was significantly reduced With cessation of fly control in the treated areas, shigella infections once more rose to almost their previous rate

Although you do not advise relaxation of efforts at fly control, health authorities unaware of this clear demonstration of fly transmission of infectious diseases might, if their funds were limited, decide that fly control could be dispensed with

We here are renewing our efforts at area fly control, and placing the emphasis on basic sanitation to prevent breeding rather than depending exclusively on residual chemical control of the adults

Ministry of Health, N G GRATZ
Jerusalem Entomologist

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[1] Watt J Lindsay D R. *Publ Hlth Rep Wash* 1948 63, 1319

[2] Lindsay D R. Stewart, W H Watt, J *Ibid*, 1953 68, 361.

LEGAL RESPONSIBILITY IN BLOOD-TRANSFUSION

SIR,—I have read with interest the article this subject by Dr James (Aug 1) In p noted the list of diseases which preclude an indi from being a blood donor These include asthma, fever, and nettlerash It seems strange that from allergic diseases migraine is omitted

This disabling complaint, said now to affect 6–8% the world's population and to be on the increase, handed down as a Mendelian dominant charac Surely it should not be transmitted indiscriminately transfusion?

London, W 1 NEVIL LEYTO

CONTRACEPTIVE TECHNIQUE

SIR,—The letters from Dr Margaret Hadley J (Aug 15) and Miss Josephine Barnes and Dr Goulding (Aug 22) give an inaccurate impression value of vaginal jelly (especially synthetic gels such 'Preceptin') as a means of contraception It is ce that conclusions on this subject should be based sufficient evidence In support of her opinion Jackson brings forward one case, she is dis because an asthmatic patient became pregnant two months of beginning to use a jelly But I c give Dr Jackson many records of cases on my files which people have become pregnant when using diaphragm and jelly and a sheath

In favour of the use of jelly without a diaphragm may cite the reports of Dr Nichols Eastman[2] of Hopkins Hospital, and Dr Alan Guttmacher,[3] American gynæcologists of high reputation who used this method In observations on 605 couples a period of twelve to thirty-six months Dr Gu found that failures due to the method numbered 0– and failures due to patients' errors numbered 0–1% total pregnancy-rate was 9 1% per 100 woman years exposure In Dr Eastman's series of 333 w observed for six months, the pregnancy rate was 16 per 100 woman-years of exposure The pregnancy when diaphragm and jelly are used together is gen accepted as between 12% and 33% per 100 woman y exposure Stromme and Rothnem,[4] in a survey reports from nearly ten clinics, found that the rate was 4% among women using preceptin compared with 12–15% among women at clinics diaphragm plus jelly, indicating a 95–98% reduction fertility during the reproductive phase

The factors which cause a method to be used re or otherwise are obviously of great importance, Dr Eastman showed that in mass studies the diap and jelly has not proved more effective than alone The ease with which the fertility control can be used may be far more important than kind of efficacy that can be judged in the laborat A suppository or a jelly can be introduced easily requires no fitting, and no repeated visits to a Moreover, Dr Goulding does not mention the uncommon circumstances in which, according to Prof Dickinson, the use of a diaphragm is contra indicated

1 In women seeking premarital advice

2 Where the size of the vagina changes frequently extensively (especially in the first ten years of life)

3 Where the woman is unable to insert or remove diaphragm—either through lack of intelligence or thr lack of facilities

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[1] Richards M G Balyeat R. M. *Genetics*, 1933, 18, 129

[2] Eastman N J Seibels R E *J Amer med. Ass* 1949, 139,

[3] Finkelstein R Guttmacher, A Goldberg R. *Amer J O Gynec* 1952, 63 661

[4] Stromme, W B Rothnem M. S *Ann N Y Acad Sci* 1 54 831

In cases of erosion of the cervix
In cases with large cystocele and rectocele

ave seen many cervical erosions in women which ned to have no other cause than the use of a phragm over a long period

think it would be true to say that the views on roductive physiology offered by the spokesman of Family Planning Association at the recent Inter ional Conference on Population and World Resources [5] not commend themselves to the Indian medical fession in India Complete objectiveness is important critical evaluation of fertility control agents

ondon, W 1   MAUNG SEIN

SHUNTING IN THE HUMAN KIDNEY

SIR,—We should like to clarify certain points raised the course of some critical comments in the current dical Annual [6] on our paper in *The Lancet* [7]

The commenter appears to accept our observations, de on some human necropsy material that the renal tex is pale and the medulla congested as demon ated macroscopically and by Pickworth s stain

he takes serious exception to our use of the term hunt' in this connection His contention is that in er to use the term, one must see the blood by passing cortex and flowing through the medulla

n our paper we had set out to collect some "*more ect* anatomical evidence of corticomedullary diversion blood *in man* " than had been forthcoming to date have not claimed that we have demonstrated shunting the human kidneys but, as morbid anatomists who re often to interpret their findings on dead tissues the basis of experimental physiological work we re read our observations as giving evidence of nting It may be relevant to note here that in the *tracts of World Medicine* [8] our observations have n interpreted as adding a valuable contribution support the hypothesis of the Oxford shunt.' We sorry to find that we have failed to give a more ir idea to some readers about what we actually meant could have disregarded the 'static distribution of od [7] after death had it not been that the paren matous damage had also a correlated distribution ch suggests that the former did not merely represent agonal picture—we could have read it simply as tical ischæmia, had it not been that the medulla more congested than normal and that the fatter false vasa recta appeared the more distinct was the tical ischæmia Nor does the reading [7] of con ions from the efferent arterioles of the juxta dullary glomeruli to the vasa recta in control pictures ative our contention. The presence of these cular channels operating normally between the tex and the medulla is universally accepted What have observed is that they become wider under se conditions, and this widening associated with the er features has been interpreted by us as *evidence* gesting the passage before death of more blood from cortex to the medulla than occurs normally—in er words of corticomedullary diversion or of shunting

We feel that the time is not yet ripe for anyone to ak too strongly either in favour of or against this ception which appears to be based on some rational ts and observations Instead one should concen e rather on the collection of further data with an n and unbiased mind

Department of Pathology
Ratan Sircar Medical College
Calcutta.

S N DE
K I SENGUPTA

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[5] See *Lancet* Sept 12 1953 p. 560
[6] Wilson C. Medical Annual. Bristol 1953 p 371
[7] De, S N., Sengupta K I *Lancet*, 1951 ii, 1100
[8] Ackroyd, A *Abstr World Med* 1952 11 431

Medicine and the Law

Name Removed from Medical List

A TRIBUNAL constituted under the National Health Service Act has directed that the name of a doctor practising in Cumberland shall be removed from the medical list of Cumberland Executive Council and shall not be included on the lists of other executive councils. This arises from the finding of irregularities in prescribing and dispensing for patients which constitute a breach of the terms of service.

The doctor, who is 31 years of age took over a practice at the end of 1948, and in October 1949 with the consent of the executive council, began to dispense for patients at a subsidiary surgery on the basis of payments according to the Drug Tariff. The offences alleged against this doctor are that (1) he dispensed or submitted to the National Health Service pricing bureau prescriptions in respect of persons (*a*) who were not included in his dispensing list and for whom therefore he had no authority to dispense (*b*) who could not be traced and who are not recorded on his list (*c*) who were deceased at the date of the prescriptions and (*d*) whose names and addresses as entered by him were illegible (2) he submitted for payment prescriptions and also duplicates thereof and where the prescription was for a quantity of drugs or appliances divided the prescription between two or more scripts, or caused it to be so divided instead of including the whole prescription in one script (3) he submitted for payment prescriptions in respect of persons on his list, which he had not actually dispensed to the persons concerned

The tribunal remarks that at least one chemist has suffered very great hardship indeed and serious financial loss through the respondent improperly dispensing his own prescriptions which otherwise this chemist would in all probability have dispensed

The doctor has not appealed against the tribunal's decision and accordingly executive councils have been instructed to give effect to it until the tribunal or the Minister of Health directs otherwise

Diary of the Week

SEPT 27 TO OCT 3

Monday 28th

CENTRAL MIDDLESEX HOSPITAL, Park Royal N W 10
5.30 P.M. Mr Gayton Brown (Melbourne): Surgical Treatment of Duodenal Ulcer by Antro-duodenectomy

Wednesday, 30th

MIDLAND MEDICAL SOCIETY
8 15 P.M. (154 Great Charles Street, Birmingham, 3) Dr W Watson Newton: Mesmer Mind, and the Emotions. (Presidential address)

Thursday 1st

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W 1
5 P.M. *Section of United Services* Surgeon Commander J S. L. Coulter Legal Problems of Modern Service Medical Administration.

ASSOCIATION OF CLINICAL PATHOLOGISTS
2.15 P.M (Westminster Hospital Medical School Horseferry Road S W 1) Opening of three-day meeting

Friday, 2nd

INSTITUTE OF DERMATOLOGY St. John's Hospital Lisle Street W C.2
5.30 P.M Prof Stephen Rothman clinical demonstration

Births, Marriages, and Deaths

DEATHS

KAHAN.—On Sept. 16 Nest Kahan (née Thomas), M.B. D.C.H D.P.M

Obituary

ARTHUR RENDLE SHORT

M D , B Sc Lond , F R C S

Professor Rendle Short, whose death we announced last week, was born in Bristol, and he spent almost the whole of his life in that city, where for many years he held the chair of surgery

His father, Mr E Rendle Short, a director of Fry's, the chocolate manufacturers, encouraged the scientific aptitudes which he showed even as a boy at the Bristol Grammar School As a student at the University of Bristol, and at University College, London, he fulfilled his early promise In 1899 he graduated B SC with first-class honours in geology, and in his medical studies he was equally successful, gaining exhibitions and scholarships, and the gold medal in the subjects of materia medica, anatomy, and medicine He took his M.B with first-class honours in 1903 and was awarded a final gold medal when he proceeded to the M.D the following year But he determined to specialise in surgery and after holding resident appointments at Bristol Royal Infirmary, and a lectureship in physiology at the university, he took the F R C.S in 1908 Five years later he was appointed to the staff of the Royal Infirmary, becoming a full surgeon in 1922 In 1932 he succeeded Hey Groves in the chair of surgery On his retirement in 1946 he was made professor emeritus

Rendle Short was an impressive teacher of the old school At the bedside he could quickly sift the essential from a mass of conflicting detail, and signpost clearly for his students the highroads of diagnosis, prognosis, and treatment He could also effectively illustrate the principles of surgery from a particular case, and his dialectical "grinds" (after the manner of a Socrates) in the pathology museum on Monday mornings cleared much clogging debris from the minds of his listeners and taught them how to go to the root of the matter Successive generations of students gratefully recall his continued interest in them One of them writes

"As a teacher Rendle Short was absolutely in the first class he tended perhaps to over-simplify the subject, but what a gift that was to harassed and bewildered students His familiar cliché—'I well remember'—pronounced in an accent which unmistakably told his hearers that he was Bristol and proud of it, became a classic with all his students and residents Some of us felt he deliberately perpetuated this characteristic intonation The term 'a physician who operates' might have been inspired by his practice While he never acquired the extreme manual dexterity of some of the greatest operators, he was a general surgeon in the best sense of the word, and as a diagnostician he yielded place to none

"The guiding principle of his life was his religious faith He never wavered in an unquestioning belief in God and the Bible A forceful, convincing, reasonable speaker who abjured polemics, he sought to carry his hearers with him by consent, and he was in great demand amongst all denominations, especially for young people Students held his first affection, and for them he travelled distances—from Finland to Hungary, from St Andrews to Southampton He used to combine a talk on a surgical subject one afternoon with a religious address in the evening An abrupt manner, almost curt at times, hid a heart which was extremely kind It seems almost incredible that we shall not see Rendle Short again, looking neat and spruce and hardly a day older than twenty years ago"

His medical writings are well known, and each in its turn has made its valuable contribution to his specialty —the *Causation of Appendicitis*, the *Synopsis of Physiology*, the *Index of Prognosis* But perhaps his main service to the profession has been his share exacting and time-demanding editorship of the *Annual* From 1919, first in partnership with the Dr H Carey Coombs, and then with Sir Henry he carried through the immense yearly task of ponding, collecting, and writing up the materi this publication Industry and superb enabled him to put twice the amount of useful into the day that most can manage, and for he also had a large consulting practice and was in d all over the West Country for his diagnostic abilit

W M C writes "Like some of the great science—Newton, Boyle, and Faraday—Rendle S was a deeply religious man and devoted himself ately, actively, and consistently to the Christian He studied recent research in all subjects relevant deeper understanding of the Bible—especially languages of the Bible, its archæology, geology, and general scientific approach To many Christian in the profession and to some who are still students has been the chief barrier to their making an and dangerous divorce between their scientific work the spiritual and moral truths of the Bible He see no necessity for any such rivalry and between true science and true religion, whether problem were looked at theologically, philosoph or scientifically Indeed, he went further From of his own strongly held and practically effective which was grounded upon a spiritual and int conviction that Jesus Christ was alone the Way Truth, and the Life, he has been the means of stabilising the Christian faith of many Ther also not a few who have through him been persua a personal faith in Christ By sheer consistency downright honesty of life, by quiet godliness abounding secret philanthropy, by an intelle clear and wholehearted confession of the Christian Rendle Short has left us a shining example of out in practice what he preached"

Professor Rendle Short died on Sept 14 at Th where he was staying with friends on his way home a conference in North Wales He leaves his wif before their marriage was a sister at the Mildmay Hospital, with a son and two daughters His daughter holds the chair of obstetrics at College in Uganda his son is a pædiatrician at and his younger daughter is a nursing sister in Nair

VALENTINE HERBERT ELLIS

M.A , B Chir Camb , F R C.S

Mr V H Ellis, orthopædic surgeon to St Hospital, London, died on Sept 15 while h finishing his morning's work in the fracture clinic he had himself planned and developed

He was born in India in 1901, the son of General Philip Mackay Ellis, O B.E , A.M.S , and h educated at Wellington and at Clare College, Cam He qualified from St George's Hospital in 1925, became F R C S three years later After hol number of junior appointments at St George's elsewhere he went as surgical registrar to the National Orthopædic Hospital at Stanmore, wh stimulus of such men as Elmslie, Laming Evans, and Trethowan quickly determined his future bent

In 1932, when he was only 30, he was appoint the staff of St Mary's Hospital, and he was the to hold the post of orthopædic surgeon there. tireless energy he set out to establish what has been leading orthopædic and fracture department. He many other senior surgical appointments, chief which were those at the Royal National Ortho Hospital, Paddington Green Children's Hospital, Lord Mayor Treloar Orthopædic Hospital at Alton the Heatherwood Orthopædic Hospital at Ascot the second world war he was in charge of the pædic unit at the E M S Park Prewett Hospital his great capacity for hard and sustained work full expression With a small but highly staff, trained by him, he dealt with an enormous of work, especially from D-day onwards During time there passed through the hospital 16,000 wo of whom many were orthopædic cases. D pressure of routine work, he found time to collect his valuable contributions on the treatment of uries of the cervical spine, the causes of failure in ne-grafting for non union of fractures and early perience in the use of penicillin His later writings luded articles in Platt's *Modern Trends in Orthopædics*, undfield Jones and Porritt's *Essentials of Modern rgery* and Fleming's *Penicillin* He was also a joint thor of *Recent Advances in Orthopædic Surgery* (1937) *He was much in demand for committee work* which undertook ungrudgingly, and he was chairman of the dical staff committee and academic board at the yal National Orthopædic Hospital In 1946 he s president of the section of orthopædics of the Royal iety of Medicine and he had served as honorary asurer of the British Orthopædic Association He s looked on as a likely choice as a future president of association.

T O A. speaks of the great loss to the specialty one of its wisest counsellors Not only was Ellis of the most distinguished orthopædic surgeons of day; he was a scholar with an exceptionally broad kground of knowledge and with interests that ranged m finance to horticulture He will be remembered the qualities which commanded respect from all affection from his colleagues and pupils—his sound mon sense, his wise judgment, his kindly humanity, quiet wit, and his loyalty

W J writes 'Valentine Herbert Ellis, known most of us as Gustav and to some few of his friends Val was quiet and reserved It was not easy to w him well but the more you knew of him the more wanted to know him Once the crust was broken friendship became very strong He was a great ker—perhaps one of the most profound thinkers the orthopædic surgeons of today Every member the select W Little Club, of which he was so long order *will agree with that, and will agree that in these* et after-dinner meetings he made his mark even more n in his important responsibilities at St. Mary's pital and elsewhere What we like to remember he earnest and thoughtful criticism that he could ays make in so friendly a way at friendly meetings.'

With his unfailing cheerfulness good nature and ly interest in affairs Valentine Ellis gave the impres , and, B H B believes, it was a true one, of ng completely happy in his life and work Indifferent naterial gain and to personal ambition he was content to the work he liked conscientiously and well. None less, distinguished appointments and recognition rally came to a man of his worth

He was keenly interested in every aspect of the are of the institutions which he served With his cial detachment and capacity to get to the essence the matter he was an effective member of committees, the number on which he served was exceptional *for these days Ellis was the ideal 'second opinion.'* wide experience careful observation wisdom, and ly helpfulness, made his advice much sought after greatly valued. We shall miss his good humoured endability and his ready and well informed con ation I think his end came as he would have ed, while engaged in the work to which he was happy ive so much of his life

r Ellis married Angela Peart Robinson in 1937 she survives him with a son and a daughter

Appointments

OONE, WILLIAM, F.R.C.S.E.: asst. surgeon, Dunfermline and West Fife Hospital.

QUIBB, J L., M.D. Brist.: asst. pathologist, hospitals in the West Suffolk area.

ELL, J V., M.B. N.U.I D.P.M.: consultant psychiatrist, pswich Mental Hospital group

TON J C. M.D Lond asst. physician, Guy's Hospital, London.

SON L. G M.B. Edin. D.A.: consultant anæsthetist, Edinburgh northern group of hospitals.

E. M., M.D. Birm.: consultant pathologist, Leicester General Hospital

LIFFE, MARY M.B. Camb. D.P.H. asst. county M.O.H., Derbyshire County Council, and M.O.H., borough of Glossop and rban district of New Mills.

TER, G V., M.R.C.S.: appointed factory doctor Alton Staffordshire.

FIELD J M M.R.C.S. appointed factory doctor Chulmleigh Devon.

Notes and News

JOURNAL OF THE R.A.M.C.

THIS journal founded in 1903 by Sir William Taylor has lately celebrated its fiftieth anniversary with a special issue[1] Earlier editors include Sir Robert Firth, Sir David Bruce Sir William Horrocks and Colonel Lyle Cummins. *Of these* Horrocks earns special mention in this festschrift, for he was editor for nearly thirty years; and a biographical note by his son, Sir Brian Horrocks, describes his work in designing mobile water-sterilisers and the box for water testing which bears his name He will also be remembered for his book on the *Bacteriological Examination of Waters* his organisation of hygiene laboratories and his chairmanship of the Anti-gas Committee during the 1914–18 war

Hygiene has always played an important part in military medicine and another paper in this issue, on the growth and development of Army barracks in the United Kingdom reminds us what excellent work military hygienists have done Clinical articles include case reports of carcinoma of the adrenal cortex causing feminism in an adult male of dystrophia myotonica and of Ganser's syndrome A survey of Service psychiatry in the Far East in 1951 the first part of which appears in this issue was written in reply to the comment of a National Service officer that except in bacteriology pathology and hygiene the scope of medicine in the Army was limited.

Nowadays fewer and fewer journals offer material that is of interest to both specialists and general readers, and it is to be hoped that this journal will soon once more be able to offer its varied contents in monthly instead of quarterly issues

CANCER DEFLATED

IN 1946 Dr I Berenblum who has spent most of his life in cancer research, wrote a book for laymen called *Science versus Cancer* which was published in England[2] He has now written a new book, also for laymen based on the former work, and first published in America last year; an English edition has now appeared.[3] In his preface he justly claims that though his approach to his subject is scientific his treatment has been as far as possible non technical. He explains the present stage of cancer research fully and fairly in words which everybody can follow, because as he says, *the ordinary reader still has but a hazy idea of what it is all* about Much of the fear which cancer inspires springs from the belief that it is a complete mystery against which patient and doctor alike are helpless. Some of this fear could be removed, we believe if the general public had a clearer idea of what is already known about cancer and Dr Berenblum rightly supposes that they will be interested to hear how this knowledge was reached. His account will reassure many anxious people because—by giving the known facts, and showing the lines along which research workers are thinking—he thins the mystery His book, in fact, reduces this disease to the level of others which lack its terrifying aura.

This is surely the type of cancer education" which Dr John Burton, medical director of the Central Council for Health Education had in mind when he said, at a meeting of the National Council of Women on Sept. 1 that knowledge is the best antidote to fear His council has suggested a scheme for cancer education, and local authorities are invited to set up small committees, under the guidance of their health departments, to discuss it This scheme is in keeping with Mr Malcolm Donaldson's[4] proposal that such local efforts should be coördinated by a central body

A DOCTORS ORCHESTRA

IN some countries the music-loving members of the medical profession have formed orchestras and it has been suggested that an orchestra should be set up in London, which might in due course perform at social functions of the profession and at charitable events. Medical and dental students doctors, dentists, and members of their families who are interested in this venture and who play orchestral instruments or who wish to help in other ways are asked to write to Dr H Ucko 14 Upper Wimpole Street London, W 1

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[1] *J. R. Army med. Cps* July 1953
[2] By Sigma Books Ltd
[3] Man Against Cancer Baltimore Johns Hopkins Press. 1952 London: Oxford University Press. 1953 Pp. 182 21s
[4] *Lancet*, Sept. 12 1953 p 565

University of Sheffield

Prof L J Witts will deliver the address at the opening session of the faculty of medicine in the Firth Hall of the university at 5 P M on Thursday, Oct 8 His subject will be the Opportunities of Medicine

British Association of Physical Medicine

The association is holding a postgraduate course in physical medicine on Saturday mornings from Oct 31 to Jan 23 Further particulars can be obtained from the hon secretary of the association, 45, Lincoln's Inn Fields, London, W C 2

Institute of Child Health, London

Prof E Husfeldt (Copenhagen) will deliver the Alex Simpson Smith lecture at 5 P M on Monday, Oct 26, at The Hospital for Sick Children, Great Ormond Street, W C 1 His subject will be Hiatus Hernia in Adults and Children

Society for Cultural Relations with the U S S R

The meeting of the society announced in these columns last week has been postponed to Thursday, Oct 22, when, at 7 30 P M, at 14, Kensington Square, London, W 8, Dr Brian Kirman will describe his recent visit to the Soviet Union

Empire Rheumatism Council

On Friday, Nov 13, at 2 P M, at 1, Wimpole Street, London, W 1, the council is holding a symposium on phenylbutazone, when the speakers will include Dr Otto Steinbrocker (New York) and Professor Domenjos (Saarbrücken) Tickets may be had on application to the secretary of the council, Tavistock House (N), Tavistock Square, W C 1

Congress of Obstetrics and Gynæcology

The fourteenth British Congress of Obstetrics and Gynæcology will be held at Oxford from July 27 to 30, 1955 The following subjects have been selected for discussion the rôle of the qualified midwife, the family practitioner, and the obstetric specialist in the conduct of normal labour, and the ætiology, prevention, and treatment of pre eclamptic toxæmia of pregnancy Gynæcological subjects will be announced later Further particulars may be had from the secretary of the congress, Maternity Department, Radcliffe Infirmary, Oxford

W.H O Regional Office for Europe

The European regional committee of the World Health Organisation, which is holding its third session in Copenhagen, has recommended that the regional office for Europe should be permanently installed in Geneva, but that the office should be housed outside the Palais des Nations where the world headquarters of W H O are established For the last two years the European Regional Office has been working temporarily in the Palais des Nations This recommendation will be submitted for approval to the W H O executive board at its meeting in January

Ophthalmological Society of the United Kingdom

The annual congress of this society will be held in the department of chemistry, University of Durham, Newcastle upon Tyne, on April 22, 23, and 24 Mr R C Davenport, Dr S P Meadows, and Prof J B Duguid will open a discussion on Inflammatory Vascular Diseases Affecting the Eyes, and there will also be short symposia on Cyclodiathermy, Changes in the Incidence of the Eye Affections of Coal miners in the Past 25 Years, and Gonioscopy Further particulars may be had from the hon secretaries of the society, 45, Lincoln's Inn Fields, London, W C 2

United States (F O.A) Research Fellowships

In response to a request from the Organisation for European Economic Coöperation, the United States government, through its Foreign Operations Administration, has provided over a million dollars to enable 150 young scientists from Europe to study in American research institutions for up to two years

About 25 fellowships will be open for award to candidates from the United Kingdom, and the Royal Society is to advise on their selection No age limits are specified but it is expected that most of the successful candidates will be between 26 and 32 years of age Applications will be considered from candidates who propose to do research in the natural sciences and in the engineering agricultural and medical sciences but excluding clinical medicine They must have a doctorate in science or equivalent experience Applications which may be made at any time will be considered at regular intervals For the first two sets of applications the closing dates are respectively Oct 1 and Nov 30 Forms of application and further information may be had from the assistant secretary of the society Burlington House London W 1

Institute of Dermatology

A series of semi permanent exhibitions will be shown institute during the winter course The first, from Oct. 24, by Miss A Gretener, will be on Medical Ill Dermatology

Foot Health Week

The Foot Health Education Bureau of the Central for Health Education, with the Birmingham health education departments, is to hold a foot health Birmingham from Oct 26 to 30, at the Midland

Abortion Law Reform Association

A meeting of this association will be held on Oct 21, at 7 P M, in the Conway Hall, Red Lion London, W C 1, to discuss the Bill to Amend the Law to Abortion. Mr Douglas Houghton, M P, and Mr Reeves, M P, hope to take part

Yorkshire Association of Graduates of University

The annual dinner of this association will be held on The guest of honour will be Mr W W Galbraith, of the Royal Faculty of Physicians and Surgeons of The hon secretary, Mr James Wishart, may be at 33, Manor Row, Bradford, 1

Princess Tsahai Memorial Fund

Mr Richard St Barbe Baker, leader of the expedition to the Sahara, is to give a lecture, on of the fund, at B M A House, Tavistock Square, W C 1, at 3 P M, on Tuesday Oct 13 Admission free, reserved seats (5*s*) may be had from the hon. of the fund, 3, Charteris Road, Woodford Green, Friends who are unable to attend are asked to send to Lord Horder, the hon. treasurer, c/o Messrs Prideaux, 9, Camomile Street, E C 3

Junior Hospital Posts

In the Sheffield region in May this year there junior hospital posts vacant, of which 31 had been for three or more months, and the regional hospital are submitting a report to the Ministry of Health out that "The present grade of Junior Hospital Officer, £700–£1000 per annum, is not an acceptable ment" The report goes on to suggest that in hospitals, or in those in unattractive areas, these posts be "weighted" by at least an additional £100 a that in hospitals which are regularly understaffed the staff should receive financial recognition of their work

N A P T Hunter Scholarships

The National Association for the Prevention of T offers to doctors and medical students four scholarships possible through the generosity of a private donor, known as the Hunter scholarships

The first is a postgraduate scholarship (£350) to enable a of a British medical school resident in the United King spend some six months abroad studying the control of tu The second is a scholarship (£350) to enable a young any medical school in the British Commonwealth outside the Kingdom to study tuberculosis in Great Britain Two scho (£150) are also offered to medical students who have been capped through tuberculosis to enable them to complete training at any medical school in England or Wales The date for applications is March 31, 1954 and further may be had from the N A P T Tavistock House North, Square, London W C 1

CORRIGENDUM *Placental Blood flow*—In the penu paragraph of Mr John Sophian s letter of Aug 15, the *increased* was omitted The sentence should read

By interpolation we are left to conclude that reduced blood flow due to myometrial tension is linked with renal biochemically detectable, in which diminished glomerular and increased renal blood flow occur

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Prof C W Asling (University of California), who has Fulbright award is spending a year in the department of of the University of Liverpool to collaborate with Prof. Harrison in research on the endocrinological factors concern arthritis in the rat

The British Epileptic Association has published a giving details of ten colonies for epileptics which will help to choose the institution best suited to their patient's Copies (1*s*) may be had from the association, 136, George London W 1

A new film, produced by the Wellcome Film Unit in collab with the Wellcome Research Laboratories describes the 'Nalorphine' (N allylnormorphine) in antagonising the morphine and other drugs with a similar action The film borrowed on application to the Public Relations Officer Wellcome & Co 183–193 Euston Road, London N W 1

VERNUTRITION AND UNDERNUTRITION

I CAUSES*

R A. McCance

O.B.E., M.A., M.D Ph.D Camb F.R.C.P., F.R.S

ROFESSOR OF EXPERIMENTAL MEDICINE IN THE UNIVERSITY OF CAMBRIDGE

rom the Medical Research Council Department of Experimental Medicine Cambridge

LECTURERS nowadays seem to make themselves famous y confounding their audiences with accounts of their test and most spectacular discoveries in subjects which re themselves only a year or two old The profundity f their investigations is usually enhanced by the nguage in which they describe them, for they never refer o any substance by its proper name if this can be coded nto a string of capital letters, sometimes followed by full tops You will realise at once that I have abandoned ll hope of achieving distinction in this way by having hosen as my title the time worn theme of ' overnutrition nd undernutrition ' and yet I feel justified in having one so for the subject is just as important as nuclear hysics or nucleoproteins The world today is facing roblems in nutrition which will not be solved by food lone (Russell 1949 Boyd Orr 1950 Dodd 1952) and n spite of our clinics for obesity the threat of famine—he greatest famine the world has ever known—hangs ver this country like the sword of Damocles (Fenelon 952 Massingham and Hyams 1953)

Much has been written about undernutrition in the st ten years, and it is quite unnecessary even if it were ssible to try to review the whole subject here Keys, rozek, et al (1950) have produced a monumental work n the subject with nearly 3000 references Lamy et al 946a–f) Hottinger et al (1948) and Helweg Larsen al. (1952) have provided detailed information about mine as it was seen in the concentration camps, and edical Research workers have given an account of ilder undernutrition as it affected the population of a erman industrial town (Medical Research Council 1951)

The unlimited amounts of food which have been ailable *to most of the industrialised and prosperous* mmunities have tempted many people in them to eat o much This, coupled with the increasing importance vascular diseases in their ageing populations, has forced th clinicians and investigators to pay attention to the bject of overnutrition. Work on obesity has been tensive for many years some of it very exact (New rgh and Johnston 1930 Moller 1931 Conn 1944 ewburgh 1944 Rynearson 1951) and new ways of ploring its effects on the composition of the body have en devised (Behnke 1942 Edwards 1950 McCance and iddowson 1951) *The results of these investigations* ve been published and are available

I have, therefore in these lectures tried to concentrate ainly on aspects of the subject which have perhaps t been fully appreciated Clinicians for instance have ways found it very difficult to accept the principles of ermodynamics, and have tried to escape from them ain and again in order to explain the weaknesses of emselves and of their fellow men There has been a dency moreover to think of overnutrition and under trition as two quite separate pathological states and little attention has been directed *towards finding* out w and where they converge into that broad and ill fined fairway of normal nutrition which lies between ry little is known about the importance of keeping strictly in the centre of this fairway and almost nothing about the possibilities of a planned departure from it The burden of my song will be calories—and to some extent proteins They are not so popular as the vitamins today but they are just as important interest in them will return

First Principles

Life as we know it consists in the metabolism and exchanges of protoplasm, and requires for its continuous existence a source of energy and a supply of nitrogenous material in some form or other to replace wastage At some period of their lives all living cells have the capacity of increasing their protoplasmic mass This constitutes growth and demands the supply or synthesis of all the protoplasmic constituents of the cell The bulk of these contain nitrogen If at any time the supply of energy exceeds their immediate requirements organisms have *the capacity of storing it, usually in the form of carbo*hydrate or fat. If the provision of energy is insufficient living creatures draw upon their store and lose weight

These basic principles are beautifully illustrated by unicellular organisms These organisms have great capacity for growth which itself creates enormous demands for energy The best way to observe them storing fat is to study them at a time when growth is for some reason limited while at the same time the provision of energy is not Growth may be restricted for this purpose by reducing the supply of nitrogenous material to the quantities necessary for the replacement of wastage. This can be done very simply in diatoms by placing them in sunlight in distilled water (von Denffer 1948–50) Nitrogenous katabolism can be neglected in such plants *if photosynthesis is allowed to go on Consequently they* lose none of their cell mass and merely deposit storage material in the form of carbohydrate and fat The same sequence of events takes place as a culture of green algæ uses up its growth promoting materials (Spoehr and Milner 1949 Fogg 1953) Some green algæ produce chemicals which accumulate in the culture medium and inhibit cell-division (Pratt and Fong 1940 von Denffer 1948) In the presence of light this leads to the storage of large amounts of fat, and the whole process can be compared with adult life in more complicated organisms. Some *Chlorellas* which were grown for me by Dr G E Fogg had an average cell volume of 80 c μ when the colony was young and 120 c μ after the cells in it had become old and fat The dry matter of an old *Chlorella* culture may contain 70% (Aach 1952) or even 85% of fat (Spoehr and Milner 1949)

If protozoa are removed from their normal environment and placed in a salt solution or distilled water they continue to swim about actively but they cannot grow They lose some of their protoplasmic mass by irreversible degradation and they dissipate much of their stores of fat In consequence they *lose weight and get very thin* Exactly the same process goes on in green algæ if they are kept in the dark. *Tetrahymena pyriformis* can be grown successfully on a synthetic medium containing a mixture of amino-acids (34%) and glucose (66%) Dr L D Hamilton and I have been studying the effect of keeping these organisms in a mixture of glucose and buttermilk which contains 16% protein 81% carbohydrate and 3% fat This diet provides a little fat and more carbohydrate than the other but much less protein Consequently it has the effect of limiting the growth rate of the organisms relative to their capacity to synthesise fat, and the result is that they get very obese (fig 1)

Adjustment of Intake and Expenditure

The drive to eat and the desire to drink are essential instincts for survival. But how are the impulses controlled ? Many writers on this subject have words hunger thirst appetite and satiety

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The first Humphry Davy Rolleston lecture for 1953 delivered before the Royal College of Physicians on May 5 The second lecture will be published in a forthcoming issue.

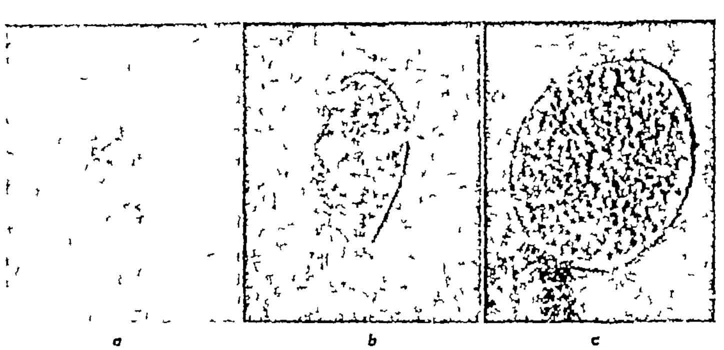


Fig 1—Effect of overnutrition and undernutrition on the protozoon *Tetrahymena pyriformis* a, after being grown on a good medium (see text) and then starved, b a normal individual grown on a good diet, c, an obese individual grown on a buttermilk glucose medium (× 1200)

closely defined (Bruch 1940), these words have such strong and such different subjective meanings that it is impossible to use them objectively A rat knows nothing about the differences between hunger and appetite, and all the work on this animal (Adolph 1947) shows that the word satiety, as we interpret it, has no place in its *modus vivendi*—yet something keeps the normal rat in water balance and calorie equilibrium People usually drink more water than they need, but there is little if any possibility of drinking too much, because all animals are provided with a mechanism for correcting this, and, no matter how great the indiscretion, the kidney can be relied upon to restore and maintain within narrow limits the volume and composition of the fluids in the fat free parts of the body The amount of water in the body, therefore, is regulated as a rule by the control of output The desire to drink, however, may not be strong enough in hot climates to keep people fully hydrated (McCance and Young 1944, Adolph et al 1947) and its complete suppression is much more rapidly fatal than a total abstinence from food No one appreciated until too late that the famous Welsh Fasting Girl would die of dehydration, but she did so long before anyone was expecting to see her succumb to a lack of food (Fowler 1871) Dehydration has been the cause of far more deaths than starvation among shipwrecked personnel and may have been responsible for some of the failures to reach the top of Mount Everest

Before discussing how the calorie balance is adjusted, it is well to say a word or two about how accurately this is usually done The food of the "average" man has often been found to provide about 3000 calories a day, but the figure varies very much from one individual to another, and in any group of 20 or more men or women, or boys or girls of the same age, there is likely to be one who appears to be eating a diet which provides him or her with twice as many calories as another (Widdowson 1947) Since both may well be maintaining their body-weights at a steady level, and since variations in digestibility and absorption may for practical purposes be neglected, it follows that the energy expenditure of different individuals must also vary How does a person know just how much food to eat to meet his own personal calorie requirements? If the "average" man takes 9 calories per day more than he requires he will only be 0 3% "out" in his adjustments Few chemical assays in the biological field have an accuracy approaching this (Wootton and King 1953), and this error would mean a gain in weight of only 1 gramme of fat a day—about 0 000014% of the weight of the body This does not sound very important, but in matters of this kind "the little more and how much it is," or (in language less poetic than that of Robert Browning) this error, if cumulative, would amount to 15 lb in twenty years This gain in body fat is possible only because the surplus fat is continually being removed from active participation in processes of the body and stored in a rel unreactive state Such an accumulation not be tolerated with an active electrolyte sodium As a matter of fact this is the sort error that most people make as they appr middle age, for the "normal" or "averag weight for a given height is about 15 lb m in the forties than it is in the twenties (Me politan Life Insurance Tables, Stern 1949) this added weight is largely due to fat (Br 1952)

Expenditure of Energy

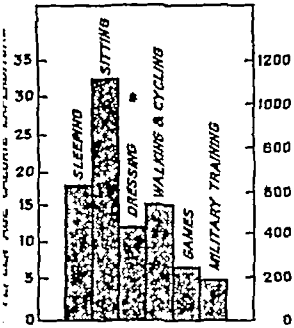
In collaboration with Dr O G Edholm, I E M Widdowson and I have recently studying the food intakes and energy exper tures of a group of active young men in train for the Armed Forces Methods have be developed recently by which the energy expenditure tasks involving *considerable muscular movement* exertion can be obtained relatively easily, and we expect more information on this aspect of prac physiology before long We were not able to apply the newer methods, but Dr Edholm pursued the and cooperative young men with pencils and paper, even from time to time with Douglas bags He could of course, keep them all under his eye for the whole the week, but he made them write down everything did during each half-hour of it Two brains may better than one for some purposes We cannot pre however, that the Edholm-Widdowson combin balanced out these peoples' calories as well as each was capable of doing it for himself, for Dr Widdow found that the young men's food provided each of with an average of 3705 calories a day, while Dr Ed working quite independently, calculated that energy expenditure amounted to 3427 calories two investigators were, therefore, nearly 300 calories on their "balance" Dr Edholm's results do, howe give us a very good idea how the calories were used The table shows the figures he adopted for som the tasks these men carried out, and the times spent on them, and fig 2 shows how the 3427 were distributed among the different occupations comparison of the two is very instructive Sleeping sitting down at lectures and similar jobs, did not re many calories per hour, but even these hours spent of time over them and they accounted for 1715 cal per day—nearly half of the total Walking and cyc about between the lectures and in pursuit of their tasks used up more of their energy than anything they did except sleeping and sitting These are rhythmical activities which can be sustained for hours end and if indulged in to any extent soon use up a number of calories Squash is a very energetic but the time spent upon it is necessarily limited,

ENERGY DEMANDS OF CERTAIN OCCUPATIONS AND AVERAGE TIME SPENT UPON SOME OF THEM

Occupation	Cal /70 kg /hr	Hr /day	Occupation	Cal /70 kg
Sleeping	60	8½	Standing	139
Sitting	112	9¼	Darts	146
Dressing changing, cleaning personal equipment &c	200	2	Snooker	156
			Cricket	154
			Running	522
			Squash	543
Walking	418	1		
Cycling	500			
Sports (as a whole)		¾		

ames as a whole only accounted for 256 out of the 3427 alories. Notice, furthermore, that more of their energy ent on dressing, changing and cleaning their personal quipment than on their practical training

The expenditure of energy is largely dictated by cir umstances and opportunity Some men have to run for twenty minutes every morning to catch their train others get to work in three quarters of an hour on a cycle while others again move mostly by car and elevator The energy men and women are called upon to expend, more over may vary widely and without warn ing from day to day Edholm found that the adets varied their *caloric expenditure during the week of* bservation over a range which averaged 775 calories per ay Stability of weight is often maintained over periods f years by an adjustment which is very exact but it is erfectly certain that the adjustment may be widely ut over short periods of time. Most people overeat, for xample on Christmas day and some of them upset eir calorie equilibrium still further on that day by aking less exercise than usual Many take violent or rolonged exercise over the weekend and few know nough about food values even to attempt to equate their eekend calories to it Animals never could. Yet a child 8 months instinctively and without direction will ake just the right amount of food for its maintenance nd growth (Davis 1928 1939) and a mouse or a rat will crease its *food* intake *to* many times its usual level uring a full lactation and drop it again immediately terwards to maintain an almost constant body weight Kennedy 1952) Observation particularly of animals hich cannot be expected to exercise any conscious ontrol of their intakes indicates that the expenditure energy is directed by opportunity external compulsion d physiological requirements The intake of energy adjusted to meet these demands. Calories are the only quirements to be met constantly like this, although at of water may be at times and if the contents of the t be regarded as lying outside the substance of the dy proper then the requirements of iron can be nsidered as being met in a similar way (McCance and iddowson 1937 1943 Hahn et al 1943) The mecha-sms by which the intake of calories is controlled must w be considered.



ig 2—Actual and percentage of total calories expended on various activities.

The Drive to Eat

In a really primitive state it was probably impossible eat too much, certainly to do so for months on end ood was too hard to come by and the time and oppor unity to eat it were lacking Enormous meals must have en taken from time to time but the fat man would on have lost the race *when survival went to the swift* Voracious desire to eat however was probably an set in the struggle Cooking must have been primitive hen there was any cooking, and food even if plentiful as probably not very easy to eat One can only eat too uch if one can get too much Obesity in other words sults from leisure and plenty It is one of the troubles of civilisation, but all civilised people are not troubled by it. A man gets too fat only when the natural control of his food intake has failed.

A desire to eat is often associated with contractions of the stomach and at one time these were thought to be the cause (Cannon and Washburn 1912 Carlson 1913 Hollander 1940) These contractions can be felt by a man and make him want to eat but dogs with their vagi cut still attack their food (Grossman and Stein 1948) and there are certainly other incentives. The nose, the eyes, the ears, and memory with everything it represents in cortical integration are all involved

When insulin had been discovered and its effects began to be explored it was soon found that one of the results of a low blood sugar was a desire *for food* Insulin has in fact been used extensively as a drug to stimulate this but its clinical effects have been attributed by some people merely to suggestion (Freyburg 1935) Mayer and his associates (Mayer 1952 Mayer and Bates 1951 1952 Mayer et al. 1952) have taken up the subject again and carried out more experimental work They believe that there is a glucostatic mechanism for regulating the intake of food Their idea is that the drive to eat, in all its manifestations, is caused by a fall in the level of circu lating blood-sugar or more precisely by a change in some high-energy bond equilibrium within some sensitive cells which depends upon this level They have shown experimentally that injecting glucose or adrenaline decreases an animal s food intake whereas insulin puts it *up and sucrose and fat emulsions are without effect* Similar experiments have been carried out by others (Hanson and Grossman 1948 Janowitz et al 1949 Janowitz and Grossman 1949), not always with the same results Mayer has also used hypophysectomised alloxan treated animals as test objects and studied the relation ship in man between arteriovenous glucose differences and the sensation of hunger which is felt only if the difference is small The ravenous urge to eat in a simple untreated diabetic he attributes to the failure of the sensitive cells to metabolise the glucose circulating in the plasma It may be added that low blood-sugars have been found in human undernutrition, and death has even been attributed to the fall (McCance 1951)

Most will agree that a case has been made out for *regarding a fall* in blood-sugar as *one* of the things that make people want to eat but there must be more Absence from food makes for generalised nervous activity of which contractions of the stomach may be one mani festation a keener sense of smell (Goetzl et al 1951–52) and irritability others. It is possible that a fall in some essential material within the nerve-cells or their end organs, rather than in the medium outside them may be the cause of the nervous activity restlessness, and reflexes which initiate the desire for food.

The Stop " Mechanism

Protozoa may be prepared to eat for twenty four hours a day and it may be impossible to satisfy their appetites if the food supplies everything that they require for growth Not so the simple hydra however which ceases to feed or to make any response to food when it has been very well filled (Buchsbaum 1953) Most animals and certainly man do not eat continuously even if they get the chance They stop I suggest, because food is one of the oldest and greatest sedatives It acts thus even in animals like hydra which possess only the most primitive nervous systems, and it does so by abolishing that activity *and restlessness which had initiated the drive to eat* There is a little experimental evidence that this is true at any rate in man; for Goetzl et al (1951–52) have found that the sense of smell becomes less keen after a meal even after one with no smell like sucrose If the effect of food is to replenish nerve-cells with oxidisable osmotic, or structural materials it is possible to explain not only the effects of a single meal but also the sustained voracity of the really undernourished (Widdowson 1951), for it may take a long time to rebuild the essential structures within the nerve cells One may recall for something comparable the length of time it takes to restore the serum cholinesterase to normal levels in people who have been undernourished (Hutchinson et al 1951) At present these ideas are but idle thoughts, for they have yet to be explored by experiment, but they may turn out to have been of some scientific value when these very fundamental problems have been solved

Little as we know about the mechanisms which restrain the primitive urge to eat, we do know a number of times and ways in which the adjustment between calorie intake and expenditure may break down A study of them tells us something about the controlling mechanisms in the higher animals and also shows us where more knowledge would be very helpful

Breakdowns in Mechanisms Normally Adjusting Intake to Expenditure of Calories

SCARCITY

Under the heading of scarcity must be classed all the degrees of undernutrition which result from economic stress, war famine, and the like These are purely physical causes, and so obvious that they need only be mentioned for the sake of completeness The same applies to the undernutrition which follows in the wake of physical diseases like cancer, particularly of the œsophagus or stomach, and other gastro intestinal abnormalities In all of these, intake fails to keep pace with requirements

PHYSIOLOGICAL REASONS

Periods of physiological overnutrition and undernutrition are part of the life cycle of some animals The young Atlantic seal, for instance, becomes extremely fat during the first few weeks of its life when it is being suckled by its mother The parent thereupon leaves her offspring to its fate on the beach and takes to the sea again, and the young seal lives on its own fat for the next few weeks before it attempts to follow its mother to the open sea and to hunt for its own food Some sea birds go through similar stages in their development, and a marmot (Morgulis 1923) may get fat enough during the summer to lose up to 40% of its weight during hibernation There seems to be a tendency for most animals to eat more than their immediate requirements if the food supply gives them the chance Perhaps the most dramatic example of physiological undernutrition is provided by the migrations of the spawning salmon, but these must be considered as bordering on the pathological, for the Pacific salmon all die after spawning Guineapigs, unlike most other animals except man, are quite fat at birth, and weaning begins at once It would perhaps be better for the young guineapigs if they were not so precocious, for most of them, in consequence, go through a fortnight or more of physiological under nutrition Most of these physiological departures from normal nutrition are entirely instinctive The higher centres are not involved Given the right conditions the results are as inevitable as they are in the protozoa

PSYCHOLOGICAL REASONS

Many people who are worried by the cares and troubles of this life find relief in eating and in the mental rest which follows it (Babcock 1948) "Fate cannot touch me, I have dined today" is the basis of a great deal of obesity Food must be compared to alcohol in this respect, and the victim may be anyone from a harassed and successful company director to a miserable and flagrantly psychopathic woman We have recently had the opportunity of studying a boy of 14 who now weighs 16½ stone (104 kg) mainly because of the psychological support he derives from overeating While he was in hospital he was given a free run of the kitchen services for a and his food was found to be providing him with calories per day Up till now all attempts to do an for him have been frustrated by his own mentality by his foolish and indulgent mother

A woman may lose all control of her food intake d pregnancy, immediately after delivery, or during tion She may eat ravenously and become immen fat in a very short time These interesting cases h been investigated by Sheldon (1949) under the gen title of maternal obesity

The very things which drive some people to prevent others from taking enough of it Worries troubles are such a common cause of a loss of wei that there is no need to elaborate on them During a continuous fast which has been undertaken f bravado, religion, or gold, the desire for food is said t pass off after a few days, but the men and women wh do this kind of thing are not psychologically normal, a this is only one example of hunger being abolished b emotion (Morgulis 1923) Sexual activity provides striking inhibitions in the animal world and may quite forcibly in man Except in psychotics and in you women with anorexia nervosa, hunger generally beg to assert itself before the undernutrition has serious It is easier to get too fat than too thin

Psychological breakdown of control clearly invol the highest nervous centres, and in man it is obvious t the cortex is an important link in the chain of contr Some patients who have had one of their frontal lo removed on account of a new growth get very f (Rylander 1939) and so also do some who have b leucotomies (Partridge 1950)

It is difficult to classify all the causes of psycho breakdown A man often puts on weight for a time af getting married, or after giving up smoking A sud change of diet from one which is bulky and of low ca value to one which is just the reverse may so dec the body and the psyche that a gain in weight is immediate result This was well illustrated by behaviour of the subjects in our Experimental Stud Rationing (McCance and Widdowson 1946) The mental diet on which the party had been living for previous three months had been a bulky one and contained very little fat At the close of the experi four persons who had become accustomed to this found themselves free to eat what they chose Th continued to eat up to the anatomical capacity of stomachs, but they replaced some of their cereals vegetables with foods like fat and sugar, of high calo value but of negligible bulk The result was that, the end of the first week of freedom came, two of subjects were found to have been eating food provid them with about 1500 calories a day more than accustomed amount—and the result was an inevit gain in weight People who have lost control for reasons usually regain it again, sometimes quite su They may merely cease to gain weight, and stabilise at a new level, or they may revert to their original we over the next year or so

A CHANGE IN REQUIREMENTS

If adult rats are confined in very narrow cages (I 1949) they become obese This has its counterpart human experience, for a person often gains weight if buys a car and ceases to take his usual exercise, or if is confined to bed with some trouble which does interfere with his appetite or metabolism The co is less common, but I know a man who regularly l many pounds of fat on his annual mountaineering hol and relied upon it to keep his corporation wit reasonable limits

In these instances one must suppose that the c in requirements failed to register on the control me n, probably because within the time of observation the ıulus was not strong enough to break through a tern of behaviour previously acquired We may ıpare the way in which quite severe dehydration may ımes be tolerated by the centres controlling the intake vater, even though it leads to a loss of bodily efficiency

AGE

ıdvancing age is probably the commonest cause of intake failing to conform to requirements Its effects obvious in both man and animals and numerous sons probably contribute to them a reduction of ivity being one The balance nearly always swings rards obesity at first and a pleasure in food may be ained until very old age but old age and all that it olves sometimes makes a man apathetic and inclined give up the struggle to provide himself with all the d he needs, but for which the zest has gone (Hobson l Blackburn 1953)

EXPERIMENTAL BREAKDOWN

d Salts

ıpart from immobilising an animal and overfeeding it removing its testes or ovaries which may produce its ects by reducing activity obesity has now been duced experimentally in a number of ways which all er scope for further study and development Brecher l Waxler (1949), for instance found that if mice were en a single large dose of aurothioglucose, about half animals lost control of their calorie intake, doubled ir weight or more, and became very fat. No lesions re found in the brain, hypophysis or thyroid, or leed in any of the other organs likely to have been ponsible. Further work will no doubt discover the nection

redity

Danforth (1927) produced a strain of mice with a nounced tendency to develop obesity The trait is ociated with a yellow colour

Danforth showed that these mice were usually rather aller than their littermates at birth and were two or ee times as heavy eighteen months later They ate more food Mayer et al. (1951) found that the obese ce tended to select a diet which contained much fat ereas their littermates chose one which was mainly rbohydrate. Guggenheim and Mayer (1952) believe at these animals have an abnormally low capacity for oxidation of acetate. This leads to an increased ilisation of acetate for the synthesis of fat. Their idence, which is based upon the use of radioactive rbon compounds is not altogether convincing Whether not there is a perversion of acetate metabolism wards the synthesis of fat Danforth (1927) showed that fat in these animals could be mobilised and oxidised ite normally if the animals were not given enough food

ırther work on this syndrome may help us to under ınd some of the cases with which we are all too familiar the outpatient departments

ypothalmic Lesions

A third way of disorganising the control of food intake s been by the puncture and destruction of two small l on each side of the hypothalamus. As with some her great advances in physiology the lead came from e clinicians (Mohr 1840 Paget 1891 1897 Fröhlich 01 Duncan 1924 Evans 1937) who described the sociation of obesity with lesions of this part of the ain Destruction of the two lateral nuclei has been found give rise to complete anorexia, and obesity has been oduced successfully in dogs cats, monkeys (Ranson al. 1938) and rats (Brobeck 1946 Brobeck et al 42–43a) by puncture of the two medial nuclei.

Immediately after the latter operation the animals hibit the most voracious impulse to eat. They gain ight with great rapidity for a time and the increase er the control animals is due almost entirely to fat. this stage they continue to provide themselves with far more calories than they require even if the food is made unpalatable by mixing it with kaolin or by giving the animals a limited amount of water Mayer (1952) has found them to have very low blood-sugars.

After a time they gradually re-establish control of their caloric equilibrium and cease to gain weight At this stage they are found to be eating no more or very little more than the controls. When they have regained caloric equilibrium after getting very fat they become distinctly 'choosey' about their food Making it more palatable leads to a further gain in weight and making it very unpalatable may cause an extensive loss of weight. At any time after operation a reduction of weight brought about by compulsory starvation or an unpalatable diet is rapidly made good as soon as the original food is restored

If normal rats are starved or undernourished for a time, they rapidly make good any weight they may have lost when they get the chance but they react quite differently to alterations in the palatability of their food for they tend to maintain a constant weight by linking their caloric intake very closely to their caloric expenditure When normal rats however, get very old and fat they tend to behave rather like the operated animals that have got fat (Brobeck et al 1942–43a, Bruce and Kennedy 1951, Kennedy 1950 1951, 1952)

The enormous intake of food of these animals after operation puts a severe strain upon their carbohydrate metabolism but they do not usually excrete glucose (Brobeck et al 1942–43b) The stored fat can be mobilised freely if the caloric intake is reduced and there is nothing to indicate that there is anything abnormal about their fat metabolism. The gain in weight and its consequences are wholly the result of eating too much food. The lesions may also lead sometimes to side-effects particularly in water metabolism (Stevenson 1940 Bruce and Kennedy 1951)

Clinicians will recognise many points of resemblance between the behaviour and pathology of these animals and of the patients who attend their obesity clinics The ravenous food consumption for a time after pregnancy; the re-establishment of control on quite a moderate intake of food but at a much greater weight, the tendency to return to this weight after it has been reduced and the fat old gourmet always looking for more palatable food and gaining weight on it may all be recognised

Cortisone

Many people treated with cortisone lose control of the balance between calorie intake and requirement (Sprague et al 1950) Hench et al (1950) reported that 11 out of 21 of their patients developed tremendous or insatiable appetites and one of them was found to be taking in 6000 calories per day Hench et al (1950) pointed out that no prediction could be made as to which patients would react in this way and that the magnitude of their response bore no relation to the benefits of the treatment on their joints. The patients all gained weight, sometimes a great deal of weight and this was in the main due to a gain in fat and muscle The retention of water and salt which might also be brought about by cortisone was a complication but only a minor one

No-one at present can say how cortisone makes people react in this way but there are two possibilities Firstly cortisone produces in some people a sense of well being and euphoria which might break down the usual critical control exercised by the cortex and make these people overeat like those who have had a leucotomy Secondly cortisone decreases carbohydrate tolerance increases the resistance to insulin and may lead to frank diabetes With the doses used by Hench et al. (1950) these effects were small and were considered to be functionally unimportant but if Mayer (1952) and his co workers are right in suggesting that the control of food intake normally depends upon the level of circulating glucose available—i e utilisable in some sensitive cells in the body—then this may be the explanation Only further work preferably quantitative work will decide

Natural Experiments

Tumours and other abnormalities of the ductless glands may break down the normal adjustment of food intake to food requirement Thyrotoxicosis always increases the demand for calories This is usually not met by an equivalent rise in intake, why not, we do not know, and a loss of weight is the result Some patients with thyrotoxicosis, however, do not lose weight and may even get fat In them, presumably, the mechanism of control remains intact and the drive to eat may even be so highly stimulated by the demand for calories that it makes the patients over react Simpson (1952) has put forward the case for the adrenals and islet tissue Ductless glands must act through their hormones—thyroxine, insulin, cortisone and so on—and the way in which these hormones act has been discussed Hormones may modify the proportions of protein, fat, and carbohydrate normally broken down, and the adrenal hormones may alter the sites in the body upon which fat is deposited, but these hormones can only induce generalised overnutrition or undernutrition by upsetting the mechanisms which normally adjust intakes to requirements They might be used more extensively to further our knowledge of these mechanisms

The Network of Control

From this jumble of observations and experimental facts it would appear that many things must be involved in the control of calorie equilibrium A few of the known ones may be

(1) A humoral mechanism depending upon the level of glucose and other metabolites in the plasma These may supply the nerve-cells with materials which produce widespread changes in activity and behaviour

(2) Fully coördinated nervous "centres" at some level in or below the hypothalamus These are normally "set" by humoral or nervous influences to produce uncontrollable hyperphagia They may conceivably be the two lateral nuclei in the hypothalamus.

(3) Two medial foci *in the hypothalamus which restrain* the activity of the centres lateral to them or below them These foci are presumably integrated with the cortex, the sense-organs, and other centres, and may also be actuated by a humoral mechanism They are essential for the physiological control of calorie equilibrium, but, judging by the behaviour of animals after their destruction, control can be re-established in their absence, admittedly only at a level of nutrition which must be regarded as pathological

(4) The cortex In man this is involved at both conscious and unconscious levels Both are extremely important, and the organs of taste, smell, sight, and hearing are naturally implicated as well—as are all the impulses arising from contractions or distention of the stomach

From the practical point of view control is ultimately conscious in most healthy people, and, if they have the knowledge and the strength of mind—and of course the means to obtain all the food they require—their weight is a matter for themselves to decide

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TREATMENT OF TUBERCULOUS MENINGITIS WITH ISONIAZID

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THE treatment of tuberculous meningitis with strepto rcin has two main disadvantages: the need for ıtinued intrathecal injections and the occasional ıcity of the antibiotic So far as the injections are ıcerned one must consider not only the long period of ess to the patient but also the possible effect of con ued interference with the cerebrospinal fluid (C.S.F.) repeated lumbar puncture introducing a foreign substance Although it is dangerous to compare an acute disease with a chronic one it is perhaps worth recalling that in meningococcal meningitis intrathecal medication—e.g a combination of serum and sulphonamide—seemed to produce less satisfactory results than did oral sulphonamide alone (Department of Health for Scotland 1944) Some workers have indeed argued that the avoidance of lumbar puncture and the use of massive doses of parenteral penicillin are of benefit despite the poor passage of penicillin into the C.S.F. (Dowling et al 1949) The discovery of the activity of isoniazid against *Mycobacterium tuberculosis* and the finding that it passed into the C.S.F. in effective amount suggested its therapeutic use in tuberculous meningitis We describe here its effects as the main method of treatment in seven cases

Material and Methods

The seven patients were unselected consecutive admissions to one unit which can exercise no control over its admissions but must accept all notified cases

TABLE I—CLINICAL DETAILS OF THE TREATED CASES

Case no	Sex	Age (yr)	Clinical assessment on admission	Isolation of *M tuberculosis*	Mantoux	Family history	Other evidence of tuberculosis
1	M	1½	Intermediate	C.S.F +	+	Mother sputum +	Snowstorm radiograph
2	F	3	Advanced	C.S.F +	+	Mother sputum +	Nil
3	F	16	Advanced	C.S.F +	+	None known	Nil
4	F	20	Intermediate	C.S.F +	+	None known	Pleural effusion
5	F	20	Advanced	C.S.F +	+	None known	Nil
6	M	3	Intermediate	Organism not isolated	+	None known	Nil
7	M	3	Intermediate	Organism not isolated	+	None	Nil

*Classified according to Medical Research Council (1948).

The first patient was admitted in July 1952 and the last in February, 1953 Every endeavour was made to confirm the existence of a tuberculous meningitis immediately after admission

The first four patients received a similar schedule of treatment During the first week in hospital streptomycin and isoniazid were both given Streptomycin was given intramuscularly and intrathecally in a dose suitable to the patient's age and weight After the first week treatment with streptomycin was stopped and thereafter the sole chemotherapeutic used was oral isoniazid 10 mg per kg of body weight daily for sixteen weeks

The fifth patient *had been treated for tuberculous* meningitis with streptomycin in the unit previously and

TABLE II—DURATION OF ABNORMALITY OF CERTAIN CRITERIA

Characteristic	Mean duration (weeks) till characteristic regained normal					
	Cases 1–4		Case 5		Cases 6 and 7	
	Isoniazid treated	Matched controls	Isoniazid treated	Previous streptomycin treatment	Isoniazid treated	Matched controls
Fever	4	9	6	40	8	8
C.S.F cells	23	34	17	54	21	42
C.S.F protein	15	37	Never normal	Never normal	14	33
C.S.F sugar	13	25	10	42	8	21
C.S.F chlorides	14	25	11	28	7	18

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was readmitted in relapse She was now given isoniazid alone 10 mg per kg of body-weight by mouth daily

The last two patients received a course of treatment similar to that of the first four, except that the duration of streptomycin therapy was increased to four weeks

In all the cases a weekly lumbar puncture was done, even after streptomycin therapy had ceased. It should be emphasised that the schedule of chemotherapy was decided at the onset of treatment and was not affected by the condition of the patient

To provide controls treated with routine streptomycin therapy, patients were selected from those treated in the unit during the immediately preceding period An attempt was made to "match" the isoniazid-treated patient with a control of similar age and severity of illness on admission Since all the treated patients have so far survived, the controls were selected from surviving streptomycin treated patients The fifth patient served as her own control

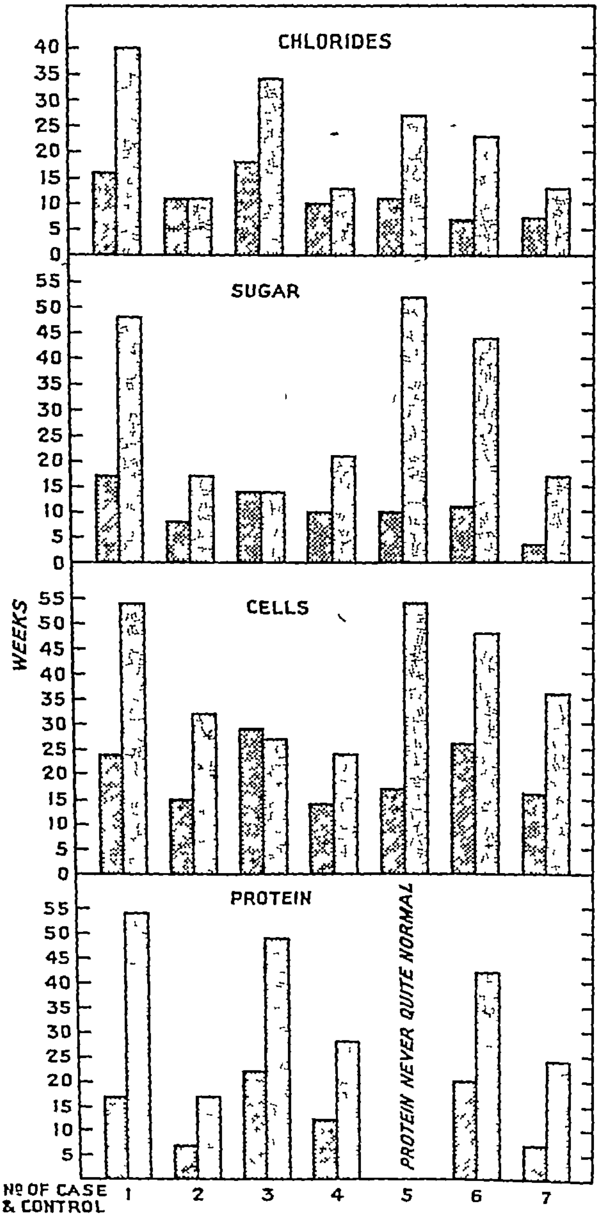

Fig 1—Alterations in amounts of certain constituents of C.S F during treatment hatched isoniazid-treated patients ; stippled, strepto- treated controls.

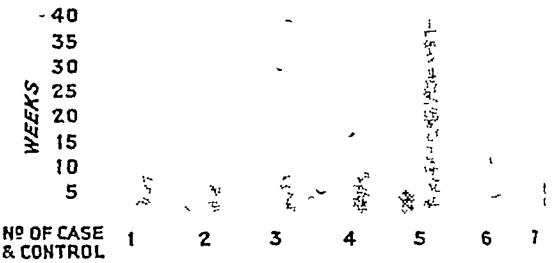

Fig 2—Time taken for temperature to settle : hatched, isoi treated patients , stippled; streptomycin treated contro

Results

Table I gives brief clinical details of the seven pati

As already stated, all the patients have surviv but the longest period of survival is only twelve mon At the present stage we have decided to use as fac of assessment the results of the serial examination of t C S F and the duration of the initial fever The follow were adopted as "normal" findings for the C (1) cells <10 per c mm , (2) protein <40 mg p 100 ml , (3) sugar >45 mg per 100 ml , and (4) chlori >729 mg per 100 ml For each patient in the series for each "matched" control the time which elap until these normal findings were reached was calcul These data are shown in figs 1 and 2, the mean fig are given in table II

Fever

The difference is greatest in the group of patients received a minimal course of streptomycin In t patients who were given streptomycin for four w the initial fever lasted much longer Although t point requires further study, it seems possible that e the intrathecal irritation produced by the strepto or the stress of repeated lumbar puncture may responsible for prolonging the fever

Constituents of C S.F

As regards all the factors chosen for comparison, isoniazid-treated patients returned more rapidly normal So far as the cells and the protein are concern such an effect may not be surprising, since any irri effect of streptomycin, with the production of an "as meningitis," was reduced to a minimum, especially cases 1–4 The more rapid return to normal of the s and chloride content is perhaps more interesting In v of the modern opinion that the chloride content is ma a reflection of the serum chloride level, the questi whether the streptomycin treated patients had persistent vomiting was considered The records did suggest that this had been a major manifestation

Although what might be termed the general pro of the patients cannot be defined in figures, all those observed the patients said that the appearance of cli recovery in those given isoniazid was very rapid appetite improved, there was obvious gain in we and even the young patients were happy and conte at a stage in the treatment much earlier than was previous experience with orthodox streptomycin ther

Discussion

We are aware that the follow-up should be lo and that our method of control is not above repr It seems, however, that isoniazid alone has pr effective in some cases of tuberculous meningitis Fur it seems that the lessened interference with the men and C S F which is possible with oral therapy may advantages in securing a more rapid return to no of the C S F chemistry There is no doubt that the arduous treatment has been advantageous in se a much happier patient and a ward whose morale turbed by the constant repetition of intramuscular and rathecal injections

We do not suggest that isoniazid alone should be garded as adequate therapy for patients with tuberous meningitis. The rapidity with which *M tuberosis* may develop resistance to isoniazid administered ne (Medical Research Council 1953) indicates a need caution, and was our reason for prolonging the course streptomycin in cases 6 and 7 Our series was so all that it does not permit any comment on this point. vertheless these encouraging results support the view at both the total amount of streptomycin and the ration of its administration might be reduced with nefit to the patient's comfort and an increase in rapidity of his recovery

Summary

Seven patients with tuberculous meningitis were given niazid by mouth as the main method of treatment l are alive after a follow up period ranging from six to elve months

The return to normal of the C.S.F constituents was ore rapid than in cases treated in the conventional y with streptomycin

There is a need to examine the best method of utilising ese chemotherapeutic agents in tuberculous meninis with the aim of reducing the amount of intrathecal terference

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TREATMENT OF TUBERCULOUS MENINGITIS

WITH STREPTOMYCIN AND ISONIAZID

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FECTIOUS DISEASES IN THE ESCUELA NACIONAL DE SANIDAD

SINCE the introduction a year ago of a new treatment r tuberculous meningitis in this hospital, a considerable ange has taken place in the clinical evolution of the sease and in its prognosis with a striking reduction in e tragic sequelæ that had so often followed in the st.

The arrival of streptomycin had already done much control this disease but treatment with streptomycin one was long tedious, uncertain and difficult, and ere could be no hope that this drug alone would solve e problem In our experience the combination of reptomycin and *p* aminosalicylic acid (P.A.S) may lead permanent cures but the prospects become much tter with the introduction of isoniazid

A Combined Treatment

In May 1952 we began to use a combination of intrauscular streptomycin oral isoniazid and intrathecal oniazid (this isoniazid was specially prepared by the stituto Ibys Madrid) We have adopted the following an to cover three months treatment

tramuscular Streptomycin

Children under 2 years of age : 0·2–0 3 g daily in one dose severe cases, up to 0·5 g

From 2 to 10 years : 0·5 g daily in one or two doses

From 10 to 15 years : 1 g daily in two doses for ten days en 0 5 g daily in one or two doses until the pyrexia subsides.

Adults 1 g. daily in two doses until the pyrexia subsides

Oral Isoniazid

Children under 2 years of age : 150 mg daily

From 2 to 10 years : 200 mg daily

From 10 to 15 years : 300 mg daily

Adults : 400 mg daily

Intrathecal Isoniazid

Children under 2 years of age : 10 mg daily in a single dose

From 2 to 10 years : 20–30 mg according to the severity of the illness.

From 10 to 15 years and in adults 30–50 mg daily, beginning with 30 mg and increasing the dose in 5 mg steps.

This scheme is only a general guide and the doses may of course be changed according to the progress of the illness and the severity of any extrameningeal lesions After more than 12 000 intrathecal injections we have observed no intolerance to this treatment or difficulty in carrying it out In all the patients generally receive in the initial treatment 30–45 g of streptomycin, 25–30 g of isoniazid by mouth and about 55 intrathecal injections—30 in the first month 15 in the second and 10 in the third

Results

The results in the first 100 cases treated with this combination have been very encouraging and there have been only 6 deaths.

Hitherto the disease had been almost invariably fatal, but we were now able to classify the cases into mild, moderate and severe forms The severity it seemed depended less on the meningeal lesion than upon any existing extrameningeal lesions and upon the constitutional resistance of the patient

Mild cases responded rapidly : in a week patients would be free from meningeal and other signs, and though the cerebrospinal fluid (C S F) was slower to respond this did not seem to affect the excellent improvement in their general condition In spite of this rapid response we continued treatment for the full three months These mild forms accounted for about 20% of cases

In the *moderate* cases progress was much slower but none the less satisfactory During the initial acute stage many patients were in deep stupor and the first sign of improvement was usually the return, at times almost imperceptible of contact with the outside world This gradual awakening was usually complete after two or three weeks but in some cases only after two months or longer The acute phase was then followed by a period of one or two months during which the patients had no symptoms of any kind, though abnormalities of the C.S.F persisted. In most patients with this moderate form the body temperature curve is typical. A febrile phase lasting over three weeks, with daily variations of about one or two degrees is followed by a second febrile phase lasting over four weeks and thereafter the patient is afebrile At the end of the second febrile phase the C.S.F is noticeably improved but it does not become normal for a further three months, during which time the patient has received no treatment whatever About 65% of cases were in this ' moderate ' group

The *severe* cases evolved more slowly and responded less satisfactorily to treatment Successive febrile phases followed each other and the general condition did not improve so rapidly as in the mild or moderate cases The persistence of symptoms and signs was often due to extrameningeal lesions especially abdominal tuberculosis The period of convalescence was much longer About 10% of cases were in this group and it is among these that deaths are to be expected

Sequelæ

The sequelæ have been mild A child with hemiplegia of the right side recovered sufficiently to move the leg muscles normally during convalescence, and though weakness of the hand muscles persisted, he could use his hand perfectly well 6 patients had paresis of the tibialis anterior, giving rise to difficulties in walking Another 3 patients dragged one foot on walking, but this improved and was not a serious disability No sensory sequelæ were noted

Follow-up

The suppression of the acute phase does not necessarily mean a permanent cure Only time will tell how efficient this treatment really is and whether the present routine will have to be modified

We have under observation 61 patients who have had no treatment for from three to seven months after the acute phase had been overcome by three months' combined therapy, 34 of them are at home and 27 are still in hospital Those at home were allowed to leave hospital because the improvement in the C S F gave grounds for confidence, and because home conditions were *satisfactory* The 27 cases *still in hospital* consist of two groups a smaller group of 6 patients who, though showing improvement in the C S F, were kept in hospital because they could not afford the journeys from their homes for monthly examination at the hospital, and a larger group of 21 in whom the C S F did not improve as rapidly as in the other cases The outlook for this second group does not seem good, and it is here that relapses have occurred The 61 cases under review are summarised in the accompanying table

RESULTS IN THE 61 PATIENTS WHO HAVE HAD THREE MONTHS OR MORE WITHOUT TREATMENT

PATIENTS DISCHARGED

Months without treatment	No of cases	Cerebrospinal fluid			Relapses
		Normal	1–15 cells per c mm	15–30 cells per c mm	
7	5	4	1	0	0
6	13	2	7	4	0
5	8	2	5	1	0
4	5	1	3	1	0
3	3	0	3	0	0

PATIENTS STILL IN HOSPITAL

Months without treatment	No of cases	Cerebrospinal fluid				Relapses
		Normal	0–20 cells per c mm	20–30 cells per c mm	Above 30 cells per cmm.	
7	8	0	4	0	4	4
6	5	0	0	0	5	2
5	10	2	3	1	4	2
4	2	0	0	1	1	2
3	2	0	1	0	1	0

The 10 relapses in 27 cases had an average clinical duration of ten days There have been no deaths

Relapses

Relapses have been mild, and in only 2 cases did meningeal signs reappear All the others were indefinite febrile illnesses with inflammatory changes in the C S F These relapses responded very well to further treatment

This raises the question of preventive treatment in all cases where the cerebrospinal fluid does not rapidly return to normal and where, four months after the completion of initial treatment, the cell count is higher than 20 Indeed, in order to be doubly sure it would perhaps be advisable for all patients to undergo a second treatment The doses, in adults that we have begun to use in an attempt to prevent relapses are 20 g of streptomycin (1 g daily), 100 mg of isoniazid by mouth in the morning 100–150 mg of isoniazid intravenously at midday, and another 100 mg by mouth at night From our experience we can confirm the effectiveness o routine

SUMMARY

A combination of intramuscular streptomycin a
*oral and intrathecal isoniazid has been used in the treat*ment of tuberculous meningitis There have been deaths in 100 cases treated in this way Of the patients who recovered, only 7 showed significant sequelæ, none of them involving serious disability There have been 10 relapses, all mild and responding promptly to further treatment

C S.F.-ISONIAZID LEVELS IN TUBERCULOUS MENINGITIS

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THE *ultimate test of any antibiotic or chemotherapeutic* régime is that of clinical trial, however preliminary observations on the concentration of antibiotic chemotherapeutic substances in various body fluids helpful in planning therapy Elmendorf et al have shown that isoniazid penetrates well into the cerebrospinal fluid (C S F) of patients with active arrested tuberculous meningitis, but the data inadequate to decide the correct dosage

The C S F -isoniazid levels found in 15 adult patients aged 16–41, with tuberculous meningitis are reported here These levels were repeatedly determined in patients throughout the course of the disease, while they were being treated with alternating high and dosages of isoniazid Present information suggests a dose of 10 mg of isoniazid per kg of body weight twenty-four hours is the highest that is likely to suitable for routine clinical use, and this level selected for the high dosage The Medical Research Council (1953a) showed that a dose of 200 mg spread over twenty-four hours regardless of body weight virtually non-toxic to patients and clinically effective pulmonary tuberculosis of adults This dose was selected for the low dosage The total 24-hour dose was administered half in the morning and half in the evening patients on the higher dosage received two or three times as much isoniazid as when they were on the lower dosage

Methods

Methods for the determination of isoniazid in body fluids are as yet imperfect To reduce error three methods were used in this investigation

(1) *Biological method* —Specimens were assayed with *Mycobacterium tuberculosis* H37Rv (human strains) as the test organism and with the media and precautions described by Medical Research Council (1948) The presence or absence growth was determined after fourteen days' incubation 37°C, specimens being assayed in duplicate, and standards run in triplicate

(2) *Method of Kelly and Poet (1952)* —The extraction an iso amyl alcohol-ether-ammonium sulphate system cribed for urine and plasma was found to be unsatisfactory when applied to C S F Specimens of C S.F, after protein precipitation with trichloracetic acid, were treated *p* dimethylaminobenzaldehyde reagent, and the resulting colour was estimated in a Spekker absorptiometer 2 cm cells and an Ilford 601 filter

(3) *Method of Cuthbertson et al (1953)* —The extraction into a butanol ether ammonium sulphate system had def advantages over the extraction procedure of Kelly and However, experiments in this laboratory showed that method of extraction did not give consistent results C S F in that with C S F containing known amounts isoniazid the extraction rate varied between 55% and relatively less material being extracted at higher concentrations Since the amount of interfering substances in C S F is less than in plasma, C.S F was directly treated

oryl chloride after protein precipitation with acid sodium ngstate. The resulting colour was read with a Spekker sorptiometer using 4 cm. cells and an Ilford 603 filter.

ERROR OF METHODS

) *Biological*

Although the biological method of assay has obvious mitations, in an investigation such as this, where the nemical methods are relatively non-specific biological ssay provides an essential check against the possibility estimating a biologically inactive metabolic derivative isoniazid.

hemical Methods

Effect of C.S.F.—Known quantities of isoniazid were ssolved respectively in water and in C.S.F. to give ncentrations ranging from 0·5 to 4·0 µg per ml and oniazid determinations were made on the specimens y both chemical methods. It was found that the alues for isoniazid were lower when the material was ssolved in C.S.F. rather than in water. The error due this cause varied from 5% to 15%. Triple determina ons were made on each specimen at each concentration y both methods; the greatest deviation from the mean ading was 10% while the average deviation from the ean reading was under 4%.

Effect of blank values.—C.S.F. after deproteinisation ves a high blank value when treated with either of the agents in question. Three separate determinations of ank values were obtained from each patient by stopping oniazid seventy two hours before the determination. ach blank value was used to correct the reading of e C.S.F. isoniazid level in specimens taken before or ter the blank determinations. The blank values by the eryl-chloride method were 0·9–2·3 µg of isoniazid per l of C.S.F. and by the *p*-dimethylaminobenzaldehyde ethod 0·5–2·0 µg of isoniazid per ml of C.S.F. The fferences between the three individual determinations r blank picryl-chloride values ranged from 0·1 to 9 µg of isoniazid per ml of C.S.F., average 0·3 µg per l.; and for the *p*-dimethylaminobenzaldehyde method om 0·1 to 0·8 µg per ml, average 0·4 µg per ml. Thus e question of the correct blank value was a matter of me uncertainty and a source of error which did not ceed ± 0·5 µg of isoniazid per ml of C.S.F. and was ely to have been about ± 0·2 µg per ml.

DIFFICULTIES WITH METHODS

Different batches of picryl chloride caused the develop nt of the reaction colour to proceed at different eeds. In most cases the development of the full colour s obtained immediately but in some cases the colour ok some hours of standing to develop.* As a routine bes were read at 2 and 12 hours to obviate this ficulty.

Certain batches of *p*-dimethylaminobenzaldehyde ected with C.S.F. in the cold. All C.S.F. in which a ld reaction colour was found was discarded, since the ferential analysis suggested by Kelly and Poet was und to be unsatisfactory.

p-aminosalicylic acid (P.A.S.) interferes with both actions, and no patient was treated with P.A.S. Both ethods were unaffected by the presence of strepto ycin in the usual concentration, but the *p*-dimethyl inobenzaldehyde reagent reacted strongly with pro ne. Piperocaine hydrochloride was used as a local æsthetic for all lumbar punctures.

Results

To ascertain whether the methods were in agreement terminations were made by all three methods on urteen specimens of C.S.F. (streptomycin had been opped seventy two hours previously to allow the biological method to be used). The biological method gave values averaging 1·8 (range 0·5–4·0) µg of isoniazid per ml of C.S.F., the picryl chloride method values averaging 1·5 (range 0·8–3·2) µg per ml and the *p*-dimethylaminobenzaldehyde method values averaging 2·2 (range 1·0–4·5) µg per ml. The '*t*' test of signifi cance showed $P > 0·1$. These figures suggested that the methods were in reasonable agreement, and that the chemical methods measured biologically active isoniazid. Further comparison between the *p*-dimethylaminobenz aldehyde and the picryl-chloride methods showed that the former gave results about 20% higher than the latter gave but when the results were tested statisti cally the difference was not significant owing to scatter.

TABLE I—RISES IN C.S.F. ISONIAZID LEVELS AT VARIOUS TIMES AFTER DOSE

Time after dose (hr.)	1–2	4–6	10–12	24
C.S.F. isoniazid level (µg per ml.) on daily dosage of 10 mg. per kg. of body-weight 12 hourly	1·4 (0·6–3·0)	3·6 (1·2–5·3)	0·6 (Detectable—1·8)	7/10 (Detectable)
C.S.F. isoniazid level (µg per ml.) on daily dosage of 200 mg. regardless of body-weight 12 hourly	1·0 (Detectable—2·8)	2·8 (1·0–3·6)	0·4 (Detectable—1·2)	4/10 (Detectable)

Each observation is the average of six readings (range in parentheses). Detectable = < 0·5 µg per ml.

Specimens of lumbar C.S.F. were withdrawn from patients 1–12 hours after a dose of isoniazid. Readings after 24 hours were taken after omitting one dose. So that the patients should not be subjected to more than the one lumbar puncture a day necessary for treatment curves showing the concentration of isoniazid at various times after a dose were constructed from samples on different days. Since there was a wide variation in the levels for any given patient, each of the points in table I was constructed from an average of six determinations on different patients, the ranges being shown in parentheses.

Table I shows that, after the oral administration of isoniazid a rise in the C.S.F. isoniazid level was apparent within 1 or 2 hours, the peak being reached within 4–6 hours. (Data confirming the peak at 4–6 hours are not given in table I, because there were only three readings at 7–9 hours.) The C.S.F. isoniazid level had fallen considerably 10–12 hours after ingestion of the dose but at the end of 24 hours isoniazid was still detectable in some patients.

Table II shows the total number of determinations done 1–12 hours after a dose. The results show a wide scatter as would be expected on the basis of the data in table I and because some of the patients being acutely ill with tuberculous meningitis, had troublesome vomiting. Patients who vomited after a dose of isoniazid were not given another dose because the purpose of table II was to show the C.S.F. isoniazid levels found in clinical practice. Analysis of the levels obtained when

TABLE II—NUMBER OF DETERMINATIONS MADE 1–12 HOURS AFTER DOSE OF ISONIAZID

C.S.F.-isoniazid level (µg. per ml.)	Not detected	0·0–0·49	0·5–0·99	1·0–1·49	1·5–1·99	2·0–2·49	2·5–2·99	3·0–3·99	4·0–4·99	5·0–6·50
Picryl chloride										
On dosage of 10 mg. per kg. of body-weight 12-hourly	—	4	4	2	2	4	13	7	6	4
On dosage of 200 mg. daily	3	8	13	10	4	5	2	—	3	2
Dimethylaminobenzaldehyde										
On dosage of 10 mg. per kg. of body-weight 12 hourly	—	—	—	2	3	—	2	4	—	6
On dosage of 200 mg. daily	—	4	3	3	7	1	1	5	—	1

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* uthbertson et al. (1953) now believe that the full colour intensity will always develop immediately provided that the picryl chloride reagent is purified by double recrystallisation from chloroform.

the patients were acutely ill and less acutely ill (excluding patients who vomited) showed no striking differences, but patients with arrested tuberculous meningitis tended to show lower levels than did those with acute tuberculous meningitis (difference not statistically significant—$P > 0·1$)

Discussion

Analysis of the data in table II shows that there was a highly significant statistical difference between the C.S.F.-isoniazid levels obtained with the two dosages These were higher ($P < 0·001$) when the higher dosage of 10 mg per kg of body-weight was given (for most patients this dosage was two or three times the amount given on the low dosage)

The 14 day inhibitory C.S.F. isoniazid level for H37Rv is 0·06 µg per ml, and it is rather generally accepted that most of the "isoniazid sensitive" bacilli will be inhibited by a C.S.F. isoniazid level 0·2 µg per ml (Medical Research Council 1953b)

Mackaness and Smith (1952) and Suter (1952) have shown independently by macrophage culture that, whereas the ratio of the inhibitory level of streptomycin for free tubercle bacilli to its inhibitory level for intracellular tubercle bacilli is 1 : 20–80, that of isoniazid is 1 : 1 This demonstration that the action of isoniazid is unimpaired when the tubercle bacilli are intracellular suggests that in-vitro tests with isoniazid may have considerable relevance to clinical treatment The action of isoniazid on the tubercle bacillus is bacteriostatic rather than bactericidal, and probably little purpose is served by having very high levels of circulating isoniazid

This contention is supported by the findings of Barclay et al. (1953) with isoniazid rendered radioactive with C^{14} in the carboxyl position These workers showed that isoniazid levels higher than the lowest inhibitory level did not lead to a greater uptake of the isoniazid by the bacilli, and that reduction of the surrounding isoniazid level caused only a slow decrease of radioactivity in the bacterial cell Isoniazid-resistant bacilli took up only minute quantities of isoniazid at all levels These findings suggest that intermittent rather than continuous bacteriostatic levels of isoniazid may suffice for optimal therapy It is realised that high C.S.F. isoniazid levels do not necessarily either imply similar levels in the extracellular spaces of the brain or indicate high therapeutic activity

Data given earlier show that if isoniazid is estimated in the presence of C.S.F., the values obtained are about 10% too low Table II has not been altered to allow for this error, since the uncertainty about the blank value makes it inadvisable to apply a correction Probably, after all allowances have been made for technical errors, levels of 0·5–0·99 µg of isoniazid per ml of C.S.F. or more in table II represent entirely adequate bacteriostatic levels of isoniazid Since some of the readings in table II were made after the patients had vomited, and since this table incorporates estimations made twelve hours after a dose of isoniazid, the figures represent a conservative estimate of the C.S.F.-isoniazid levels likely to be obtained

The 12 patients treated with 10 mg of isoniazid per kg of body-weight daily showed no evidence of toxicity due to this dosage for 4–8 weeks

Table II shows that a dosage of 200 mg daily in adults regardless of body-weight gives rise to C.S.F.-isoniazid levels that appear on theoretical grounds to be desirable, though the adequacy of this dose can only be established by clinical trial

Debré and Brissaud (1952) have suggested that isoniazid should be administered both orally and intrathecally in tuberculous meningitis The findings in the present investigation suggest that intrathecal isoniazid

Summary

The C.S.F.-isoniazid levels were estimated in 15 with tuberculous meningitis in all stages of the The patients received alternating high and low of isoniazid

The two chemical methods used were checked a biological method to show that the chemical measured active isoniazid and not an inert metab derivative

Adequate bacteriostatic C.S.F. isoniazid levels found on both dosages throughout the illness

I wish to thank Dr W F J Cuthbertson, of the Gl Research Laboratories, and Dr S W A. Kuper, of Brompton Hospital, for providing me with details of picryl chloride method for the determination of isoniazi and Mr J Tobar for technical assistance in the laboratory

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ANÆMIA ASSOCIATED WITH HÆMOPHILUS INFLUENZÆ MENING

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IN a survey of 1069 histories of acute meningit infants and children admitted to the Children's H Melbourne (Rubbo et al), our attention was draw the extensive use of blood-transfusions in *Hæmo influenzæ* meningitis This observation led to examination of the frequency and severity of in this disease and in meningococcal meningitis. T results are presented here

Investigation

It is generally recognised that 50–60% of an infants and children are secondary to infection (1947, Diamond 1950), but significant anæmia has usually been observed in acute infections of less th month's duration (Cartwright and Wintrobe 1952) finding of a frequent association of anæmia with infl meningitis clearly shows that this complication may

TABLE I—STANDARDS USED FOR CLASSIFYING DEGREE ANÆMIA IN CHILDREN

Age group	Normal Hb level (g per 100 ml)	Degree of anæmia		
		Mild < 85% of normal (g per 100 ml.)	Moderate < 75% of normal (g per 100 ml)	Severe < 65% (g. per 100
0–3 mos	15 (*104%*)	11·9 (*82%*)	10·5 (*72%*)	9·1 (
4–12 mos	12 (*83%*)	10·2 (*70%*)	9·0 (*62%*)	7·8 (
13–24 mos	12·5 (*86%*)	10·6 (*73%*)	9·4 (*66%*)	8·1 (
2 yr or more	13 (*90%*)	11·0 (*76%*)	9·8 (*68%*)	8·5 (

Hb in peripheral whole blood 14·5 g per 100 ml = 1

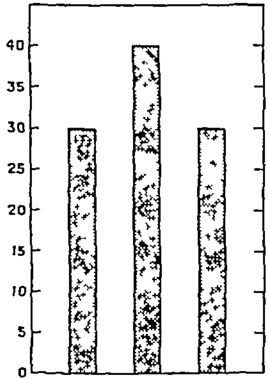
TABLE II—ANÆMIA IN ACUTE MENINGITIS IN CHILDREN

Ætiology	No. of cases	No. of cases with anæmia	Cases given blood transfusion (%)
influenzæ	196	89 (45·4%)	37·7*
meningitidis	141	11 (7·8%)	1·3

ncludes 11 cases given blood transfusions but not included in anæmic group because Hb estimations were not recorded

served in acute, as well as in chronic infections. Apart om isolated statements such as that of Turner (1948) io reported that 7 of her 40 cases of *H. influenzæ* eningitis required blood transfusion, the association of æmia with influenzal meningitis seems to have escaped tention. We report here the results of a study of 208 cteriologically proven cases of *H. influenzæ* meningitis, which 196 were consecutive cases admitted to the ildren's Hospital in 1946–52. For comparison, we fer to a series of 141 cases of meningococcal meningitis eated in the same hospital over the same period.

It was appreciated at the outset of this study that any timate of the frequency of anæmia would depend on the emoglobin level chosen as the criterion of anæmia. e level chosen was 85% of the expected normal level ter correction for the patient's age in the peripheral blood, 14·5 g. of hæmoglobin per 100 ml. of blood being taken as equivalent to 100% hæmoglobin. The hæmoglobin levels for assessing the degree of anæmia in various age groups are shown in table I.



g 1—Severity of anæmia in 89 cases of *H. influenzæ* meningitis.

Results

With this classification 89 of the 196 consecutive patients with *H. influenzæ* meningitis (45%) were anæmic on admission to hospital or developed anæmia within seven days of admission. This surprisingly high icidence is probably a conservative estimate for it does ot include 14 patients who received blood transfusions r the many patients given oral iron therapy who were ot classifiable because hæmoglobin estimations were not corded. In contrast the incidence of associated anæmia meningococcal meningitis was 7·8%. These differences able II) suggest that anæmia of meningitis may be eculiar to *H. influenzæ* infection.

As regards the severity of this anæmia, fig. 1 shows at in 70% of the anæmic patients the anæmia was oderate or severe—i.e., the concentration of hæmo obin was less than 75% and 65% of the corrected normal alue respectively. In some cases the anæmia was well elow these critical values and in 10% (18 patients) the emoglobin was equal to or less than 7·3 g. per 100 ml. g. 2).

Thus, anæmia in *H. influenzæ* meningitis is not only equent but also moderately severe. From the clinical andpoint it can be easily corrected and, if recognised, does not appear to affect the prognosis, particularly ith the modern chemotherapeutic control of the meningitis. In 1946–52 the over-all case-fatality rates among anæmic and non-anæmic patients were 14·3% and 13·2% respectively.

The mechanisms causing anæmia during infection fall broadly into three main groups—aplasia of hæmopoietic tissue, intravascular hæmolysis, and maturation arrest in the synthesis of hæmoglobin (Saifi and Vaughan 1944). We cannot offer any experimental evidence of its significance in *H. influenzæ* infection, but the following observations are relevant.

There appears to be a definite relation between the degree of anæmia and the severity of the infection measured by the concentration of glucose in the cerebrospinal fluid (C.S.F.) (Alexander 1943). This relation is brought out in table III, which shows that anæmia was present in 57% of all severe infections (C.S.F. glucose level below 10 mg. per 100 ml.), in 40% of moderate infections, and in 30% of mild cases.

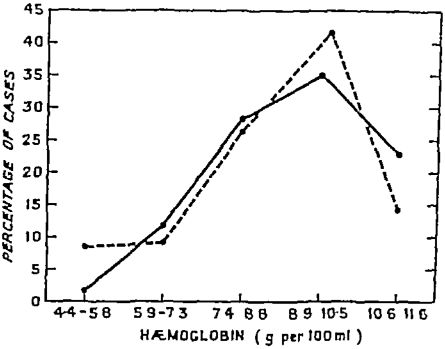


Fig. 2—Effect of serum therapy on degree of anæmia in *H. influenzæ* meningitis: solid line, 54 cases without serum therapy; interrupted line, 35 cases with serum therapy.

That the age of the patient did not affect the frequency of the anæmia was shown by the almost identical age distribution of anæmic and non-anæmic patients: 69% of all the patients and 71% of the anæmic patients were aged less than 1 year.

The blood-group of the patient had no apparent influence on the incidence or degree of anæmia; for a normal distribution of blood-groups A, B, O, and AB and of the Rh factor was found among the anæmic patients.

It was impossible, with the information available, to determine whether an incipient anæmia of dietary or other origin preceded, or was aggravated by, the infection. Most of the patients came from the industrial (lower economic class) areas of the city, but the same social distribution applied to cases of meningococcal meningitis in which anæmia was uncommon.

The question was raised whether the administration of type-b rabbit antiserum might be causally related to the development of anæmia. That this was not so is shown in fig. 2, in which the degree of anæmia in two groups of

TABLE III—RELATION BETWEEN DEGREE OF ANÆMIA AND SEVERITY OF INFECTION IN H. INFLUENZÆ MENINGITIS

Degree of infection	C.S.F. sugar level (mg. per 100 ml.)	No. of cases	Association with anæmia (%)				
			None	Mild	Moderate	Severe	All grades
Severe	< 10	76	43	17	16	24	57
Moderate	10–30	30	60	17	23	0	40
Mild	30–50	24	80	8	4	8	36

anæmic patients, one group treated with the antiserum (usually intramuscular) and the other not, showed much the same distribution Thus there was no evidence that serum therapy induced hæmolysis or agglutination, thereby increasing the severity or precipitating the anæmic syndrome

Discussion

We have been able to show that anæmia is often associated with *H influenzæ* meningitis but seldom with meningococcal meningitis (table II) This finding is of some interest in so far as many hæmatologists consider that significant anæmia is not seen in acute infections of short duration The frequency of the association in 196 consecutive cases was 45%, after the exclusion of those patients whose hæmoglobin levels were not recorded but who were treated by either blood transfusion or iron therapy A conservative estimate would be that half of the cases present with anæmia or develop anæmia during the illness, and in 70% of these the anæmia is moderate or severe (fig 1) In the present series two-thirds of the anæmic patients (38% of all the patients) were given blood-transfusion (table II) Whereas the severity of the anæmia was partly influenced by the severity of the infection (table III), age, blood-group, social class, and antiserum therapy (fig 2) did not affect the incidence or the severity

The question whether the anæmia was a predisposing cause or the result of specific infection is entirely open We noted that the anæmia often developed during the course of the illness, and not infrequently the hæmoglobin level rapidly fell in twenty-four to forty eight hours These sudden changes seem to indicate that mechanisms involving intravascular hæmolysis are at work during infection Unfortunately no complete observations on pigment balance were recorded in the histories A tentative suggestion is that sensitisation of the cells by *H influenzæ* polysaccharide (Keogh et al 1947) might lead to subsequent hæmolysis by a naturally occurring lytic component (e g , complement) or by chemotherapeutic agents in circulation (e g , sulphonamides)

Summary

An analysis of 196 consecutive cases of *H influenzæ* meningitis in infants and children revealed that 45% had an associated anæmia, and in 70% of these the anæmia was moderate or severe In contrast, the incidence of an associated anæmia in 141 cases of meningococcal meningitis was only 8%

The anæmia was more frequently associated with the severer forms of meningitis but was not related to the patient's age, blood group, or social class, or caused by the administration of type b rabbit antiserum

From a clinical point of view this association with anæmia should always be considered in the management of *H influenzæ* meningitis The anæmia did not affect the fatality rate, probably because it was recognised and treated (two thirds of the anæmia patients were given blood transfusions)

Possible mechanisms and the significance of anæmia in *H influenzæ* meningitis are briefly discussed

Our thanks are due to Miss A. A. Robbins, of the records office of the Children's Hospital, Melbourne, for her coöperation, to Dr V L Collins, medical director, for giving us access to case histories, to our colleague Miss Patricia Gladwell, and to the Medical Research Funds for a grant to one of us (D J S)

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LACTOSURIA AND GLYCOSURIA IN PREGNANCY AND THE PUERPERIUM

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The application of paper partition chromatograp (Consden et al 1944) to the identification of sugars i urine, first described by Horrocks and Manning (194 marked an important advance in clinical chemistr Conventional methods of identification of urinar reducing substances by yeast fermentation and osazo formation are notoriously insensitive in practice an often yield equivocal results Paper partition chro graphy enables reducing substances to be identified certainty even when present in low concentration, the presence of more than one sugar may be shown by single test

With the introduction of this technique in our labor tory lactosuria was found to be very common in pr nancy, being more common than glycosuria Since th finding was at variance with current views, it was th desirable to reinvestigate the occurrence of lactosur and glycosuria in pregnancy

The frequent occurrence of glycosuria during pregnan is generally recognised , indeed its appearance after dose of glucose was at one time suggested as a diagnos test for pregnancy (Welz and Van Nest 1923, Hirst a Long 1926) Lactosuria has been known to occur dur lactation since Hofmeister (1877–78) first isolated lacto from urine, but most of the standard textbooks of clin chemistry emphasise the rarity of lactosuria befo delivery (Bodansky and Bodansky 1952, Cantarow a Trumper 1949, Duncan 1947, Harrison 1947) Hard et al (1947), however, state that lactose is found in th urine in pregnancy, and Peters and Van Slyke (194 mention that it is not uncommon to find traces of l in the later months of pregnancy

Reference to the earlier reports about lactosuria befo delivery shows lack of agreement

Lemaire (1895–96) identified lactose in the urine dur lactation by osazone formation, but before parturition could only detect glucose

Porcher and Commandeur (1904) identified lactose in th urine of a few women both before and after delivery

Williams and Wills (1928), using the osazone metho found no lactosuria before delivery in 21 clinically norm pregnancies in which sugar was present in the urine

Watkins (1928) claimed to have shown that small quantit of lactose were constantly present in the urine during th last stages of pregnancy, and that its excretion was sudde increased just before delivery , however, he did not identi the sugar but assumed that increase of the non fermentabl reducing substance represented lactose

Winter (1931), who recognised lactose by increased reducti after controlled hydrolysis as well as by the optical rotati and melting point of the isolated sugar, found only glucos in the urine before parturition and only lactose after deliver

Brock and Hubbard (1935) used a method of great sensiti and specificity to estimate the urinary sugars, determin the reducing power colorimetrically after differential bacteri fermentation , they showed lactose to be present in sma amounts in a large proportion of pregnant women, even in the early months

Archer and Haram (1948), using Fearon's methylam test found not a single positive test for lactose in 777 a specimens of urine from 123 patients, although lactose w found in the urine of 86 of 97 postnatal patients

Odin and Werner (1950), using paper chromatograph demonstrated lactose in the urine of 9 of 10 pregnant wome (Zilliacus and Roos 1952), also using paper chromatograph found lactose in the urine of 21 of 83 pregnant women, in case as early as 3 months

Clinical Data

ntrol Patients

Single specimens of urine were obtained from 372 selected patients, 240 non pregnant females and 132 ales, to act as controls Most of these specimens were om inpatients and outpatients attending University llege Hospital, but a few were obtained from healthy ung adults The age-distribution of these patients and e time of voiding the specimens were not standardised

ntenatal Patients

Specimens of urine were obtained from 245 patients tending the antenatal clinic of the hospital These tients were unselected in that they were booked nsecutively in the antenatal department, an undue oportion of primigravidæ is included because these e given priority for admission Specimens were obtained om each patient at every attendance at the clinic—i e rmally at the first attendance and then at monthly tervals until 32 weeks fortnightly between 32 and 36 eeks and thereafter weekly No specimens were tained before the 8th week of pregnancy Usually erefore, 12 specimens were expected from each patient . practice the full quota was not always obtained cause of either non-attendance at the clinic or failure to llect the specimens Specimens from patients attending e morning and afternoon clinics were voided between and 10 30 A.M and between 1 and 2 30 P.M respec vely The following details were abstracted from the tients antenatal notes date of last menstrual period e number of previous pregnancies, number of live rths, and whether the patient had diabetes mellitus any form of pregnancy toxæmia. The duration of egnancy was calculated from the first day of the last enstrual period In only a few instances were these lculations corrected when clinically this date was nsidered to be a month out

stnatal Patients

Clean specimens of urine were obtained from the tients followed antenatally on the second fourth and ghth days after delivery while in hospital and later at weeks and at any subsequent attendances at the stnatal clinic The former specimens were voided out 6 A.M and the latter between 1 and 3 P.M

Methods

Every specimen of urine had its specific gravity termined and was submitted to a qualitative Benedict st and to chromatographic analysis. While awaiting romatography it was stored at 4°C

ecific Gravity

This was measured with specific-gravity beads, the me set being used for all the determinations

alitative Benedict Test

This was performed and assessed in a standard manner follows:

Exactly 0 5 ml of urine and 5·0 ml of Benedict s qualitative agent (Benedict 1908–09) were pipetted into test tubes and ixed by shaking The rack holding the tubes was lowered to a boiling water bath for 5 minutes. On removal any red ange yellow or obvious green reductions were recorded as ch. Green reductions were subdivided into green 2 and green according to whether the colour was a yellowish green or a uish green. Thereafter the tubes were allowed to stand until dimentation was complete The precipitate was then amined in those tubes as yet ungraded; if there was none if it was grey the test was recorded as blue (or negative) hereas if any yellow component was present reduction was corded as green 1 With this technique the sensitivity of e test was such that glucose and lactose added to urine hich had previously not reduced Benedict s reagent could be tected in concentrations as low as 10 and 15 mg per 100 ml spectively

Chromatography

The general technique of Horrocks and Manning (1949) was followed with some modifications

As a routine 20 µl. of urine was spotted on the strips of filter paper; occasionally 40 µl or more was applied when the urine was unusually dilute Since absolute temperature control could not be achieved, marker strips spotted with known sugars were run at the same time to establish the R_f values under the prevailing conditions Normally the 4 : 1 : 5 n butanol acetic acid water solvent of Partridge and Westall (1948) was used but since this solvent does not separate lactose from maltose and glucose from galactose one or two specimens of urine from each patient were also run with the collidine lutidine-water solvent used by Dent (1948) for amino acid chromatography The latter solvent separates these pairs of sugars widely but, since the colour of the sugar spots is not so intense 80 µl of urine was applied to the strips developed with this solvent Immediately after develop ment of the colour the quantity of the sugar present was estimated by visual matching of the spots with standard charts. These permanent colour charts, one for lactose and one for glucose were constructed by carefully matching spots obtained on standard chromatograms. The accuracy of this method of estimation was determined by running 200 strip chromatograms spotted with a complete range of sugar concentrations it was shown that 75% were correctly assessed to within ±33% of the actual value of the colour standard

The spray reagent used to show up the reducing sugars on the chromatograms is prepared by dissolving 1·25 g of *p* phenylene-diamine and 3·0 g of stannous chloride in 200 ml of ethyl alcohol and 50 ml of glacial acetic acid. After standing for half an hour the reagent is filtered Normally it was used three hours after preparation but it will remain stable at room temperature for two or three days. The incorporation of stannous chloride delays the appearance on the paper of a background colour which develops after the paper has been heated or exposed to light. After the freshly sprayed chromatogram has been heated in an air oven at 105°C for 15 minutes hexoses show up as brown spots and glucuronates and pentoses as red spots; urates do not react. The intensity of the colour reaction with this reagent is such that lactose and glucose can be detected in concentrations of 17 and 14 mg per 100 ml respectively when 20 µl of the solution is applied to the chromatogram run with the n butanol-acetic acid water solvent

Analysis of Results

The clinical and laboratory data were analysed with the aid of punch cards. The urinary findings were grouped as indicated in the accompanying tables and figures Where more than one specimen of urine from a given patient was examined in a particular period—e g 34–35 weeks inclusive—the results were averaged before transference to the cards. Since 24-hour specimens of urine were not available, the quantitative sugar values were corrected for the variable dilution factor of the specimens by referring the figures to an arbitrary standard specific gravity of 1·020 Thus a urine of sp gr 1·010 assessed as containing 150 mg of lactose per 100 ml would on correction be assigned a concentration of lactose of 300 mg per 100 ml.

Results

Results of Benedict Tests

The over-all results are given in table I which shows that the frequency of urines giving positive reduction tests in pregnancy is about 2½ times and in postpartum patients about 3 times that in the controls They also indicate that it is only in the puerperium that the incidence of the heavier reductions of Benedict s solution is much increased

The results of the Benedict tests at different stages of pregnancy and the puerperium are further analysed in fig 1 It will be noted that the percentage of specimens giving no reduction falls from about 40% at 8–11 weeks to about 21% at 40 weeks. The other notable change is the increase in the incidence of the heavier reductions which begins at about 28–31 weeks and persists until

TABLE I—OVER ALL RESULTS OF BENEDICT TESTS

Source of urine	No of specimens tested	Percentage of negative Benedict tests	Percentage of positive Benedict tests		
			G_1	G_2	Ye & Or
Female controls	240	71 3	25 4	3 3	
Male controls	132	64 4	31 1	4 5	
Antenatal patients*	2373	27 1	68 5	3 9	0 5
Postnatal patients*	657	12 2	69 2	17 7	0 9

* The findings in one patient, shown subsequently to be mildly diabetic are not included

delivery On the second day of the puerperium there is a slight increase in the incidence of reductions, by the fourth day only 2 4% of specimens show no reduction and 35% show heavy reductions Six weeks after delivery 10% still show a green-2 reduction

Chromatography Results

The over all results are shown in table II The collidine lutidine runs showed that in no case was maltose or galactose present in those urines examined

It will be noted from table II that about 9% of the controls, both male and female, had detectable quantities of lactose in their urine, and that lactosuria was found at no less than 50% of the antenatal patient attendances, the frequency of lactosuria being double that of glycosuria The other notable finding is the remarkably low incidence of glycosuria after delivery, an incidence even lower than that found in the controls

The chromatography results in the pregnant women are further analysed in fig 2 These results show that

(1) The incidence of lactosuria increases steadily from the third month of pregnancy until 34–35 weeks, when 64% of the patients show lactosuria Thereafter there appears to be no significant change

(2) Lactosuria is more common after delivery, 99% of patients having detectable quantities of lactose four days after delivery

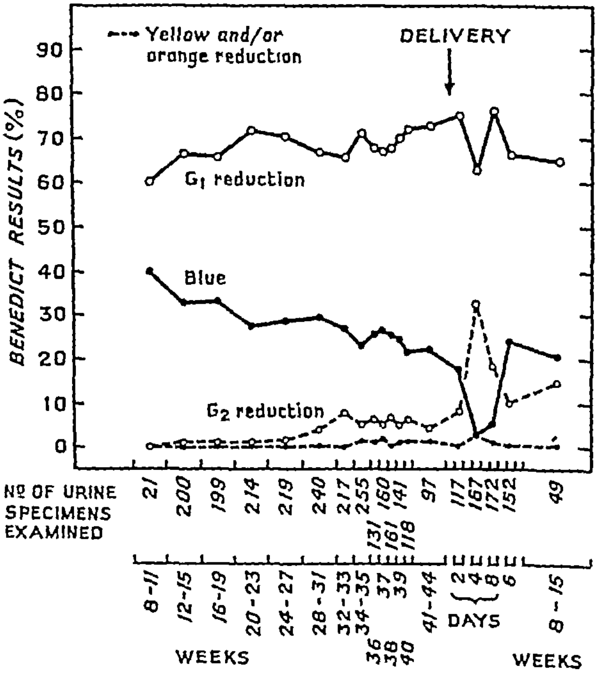


Fig 1—Results of Benedict tests at different stages of pregnancy and puerperium Blue = no reduction

(3) The amount of lactose excreted is usually less t 100 mg per 100 ml before delivery and more than 100 mg 100 ml during the early puerperium

(4) The incidence of glycosuria rises sharply after the month and fluctuates between 20% and 31% for the remai of the pregnancy

(5) The glycosuria of pregnancy disappears abruptly delivery, no urinary glucose being found on the eighth after delivery or thereafter

(6) The quantity of glucose excreted during pregnancy usually less than 67 mg per 100 ml

(7) After 16–19 weeks' pregnancy lactosuria is m common than glycosuria

To discover the constancy or otherwise of lactose glucose excretion during pregnancy, the findings in patients from whom specimens were obtained at ten more of the antenatal attendance periods (weeks 41 counting only as one attendance period) were analys In only 8 (6%) of these patients did lactosuria no

TABLE II—OVER ALL RESULTS OF CHROMATOGRAPHIC ANALY

Source of urine	No of patient attendances	Percentage of patient attendances with lactosuria found (with or without glycosuria)	Percentage of patient attendances with glycosuria found (with or without lactosuria)*	[illegible]
Female controls	240	9 6	14 2	[illegible]
Male controls	132	8 3	15 9	[illegible]
Antenatal patients	2174	50 0	24 0	[illegible]
Postnatal patients	649	86 2	0 9	[illegible]

* The findings in one patient, shown subsequently to be diabetic, are not included

occur, whereas 42 (33%) never had glycosuria at time Lactosuria was found at every antenatal atten in 5 patients (4%) and glycosuria constantly in 3 pati (1 of these 3 patients was subsequently proved to mild diabetes mellitus) Of the 119 patients who show lactosuria, lactose was detected in 61 (51%) on six more occasions, whereas of the 85 who showed glycos in 42 of the patients (49%) the sugar was detected on one or two occasions In most of the patients, the fore, lactosuria and glycosuria occur as [illegible] phenomena

Investigation of Mechanism

In an attempt to elucidate the mechanism respons for lactosuria and glycosuria in pregnancy the incid of the excretion of lactose and glucose was compared groups of patients selected from the 127 from whom or more specimens had been obtained In every case groups compared consisted of the maximum of pa in whom the incidence of all but one of the foll variables was identical age group (under 20, 20- 25–29, 30–34, 35–39, 40 or more), number of prev abortions (0, 1, or 2), number of children (0, 1, 2, or m than 2), clinics attended (A M or P M.), occurrence toxæmia (no toxæmia, slight pre eclamptic toxæ definite pre eclamptic toxæmia, or essential hyp tension) The results are shown in tables III–VI "distribution correction" in these tables shows to wh extent the differences found are likely to be attribut to the groups not being exactly similar in terms numbers of specimens examined at particular periods pregnancy Thus, in table III part of the difference in over all incidence of lactosuria between the two groups due to the fact that 8 of the A M clinic patients atten at 8–11 weeks (when the expected incidence of lacto is only 9 5%) and 6 at 41–44 weeks (when the expe incidence of lactosuria is 53 2%), whereas only 1 of P M clinic patients attended at 8–11 weeks and 11 41–44 weeks fferences due to such inequalities are eliminated The rrection factors were calculated from a knowledge of) the numbers of patients providing specimens at rticular periods of pregnancy, and (2) the expected cidence of the sugar excretion at each particular riod (fig 2)

In table III the effect of the time of day on sugar cretion is shown It can be seen that the incidence of ycosuria, and to a lesser extent of lactosuria, is higher the patients attending the afternoon clinic

In table IV the effect of previous pregnancies is shown his table shows that the incidence of the excretion of oth sugars is lower in those who have borne children his finding was elaborated by *comparing the results in* ree groups of 10 patients with no children with one ild and with more than one child. The results con med the above mentioned finding and suggested that e incidence of lactosuria diminishes with increasing mbers of successful pregnancies, the corrected per ntage *of patient attendances with lactosuria being* 3·0 50 5 and 31 7 respectively

In table V the effect of age is shown From these data seems that age has no effect on the incidence of lacto ria, but that the frequency of glycosuria probably creases with age

In table VI a comparison is made between a group of 4 patients with toxæmia and a similar group of 44 *ithout any form of pregnancy toxæmia Of the patients* ith toxæmia 4 had definite pre-eclamptic toxæmia requiring admission to hospital, 4 had essential hypertension, and the remaining 36 had only a slight degree of pre-eclamptic toxæmia as defined by Browne (1947) *The results show that there is no connection between* the milder varieties of toxæmia and sugar excretion in pregnancy

TABLE III—COMPARISON OF SUGAR EXCRETIONS IN PATIENTS ATTENDING MORNING AND AFTERNOON ANTENATAL CLINICS

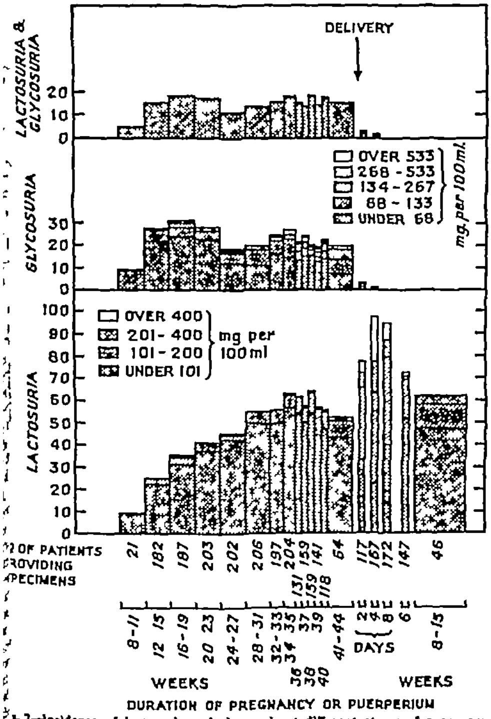
—	Patients attending		Distribution correction for P.M clinic group
	A.M. clinic	P.M. clinic	
No of patients in group	24	24	
No of patient attendances	262	267	
Percentage of patient attendances with lactosuria	42 7	51·4	−1 7
Percentage of patient attendances with *glycosuria*	14 1	25 8	+0 4

It is well known that postnatal lactosuria and lactation are related but it was noted that lactose excretion occurred quite frequently in mothers not feeding their infants. Because of this we compared the incidence of lactosuria in breast feeders and in non breast feeders *The results are shown in fig 3, the number of patients* concerned being shown in table VII The small number of non breast-feeders makes comparison of the two groups unsatisfactory However it seems that the incidence of lactosuria up to eight days after delivery is comparable in the two groups although lower concentrations of lactose were found in the urine of the non breast-feeders The incidence of lactosuria six weeks after delivery is about three times as great in breast-feeders

Discussion

Results of Benedict Tests

The results recorded here confirm the well established fact that the concentration of urinary reducing substances is often increased in pregnancy and the puerperium However the incidence of urine giving positive Benedict tests is considerably in excess of that recorded by other workers in the controls and antenatal and postnatal *groups* (*Williams and Wills 1928* Richardson and Bitter 1932 Brock and Hubbard 1935 Weidin 1948) The results obtained by Archer and Haram (1948) are nearest akin to ours they found reduction by 64% of 777 specimens of antenatal urine 81% of 258 speci mens of postnatal urine, and 11% of 503 control specimens of urine The discrepancies are probably due *to differences in technique Precise* measurement of the urine and reagent, use of a boiling water bath for 5 minutes and standing the tubes until sedimentation is complete are particularly important if small quantities of reducing substances are not to be missed The importance of technique is shown by the differing opinions on the sensitivity of the test; Watkins (1928) found that urine with more than 150 mg of sugar per 100 ml usually gave a positive test, whereas Brock and Hubbard (1935) and Weidin (1948) found that all urine with 60 mg or more of glucose per 100 ml. gave positive tests. Most textbooks of biochemistry state that the test will detect glucose down to a concentration of 100 mg per 100 ml. We were surprised to find that we could detect lactose and glucose at much lower concentrations. In this connection it is significant that sugar was



2—Incidence of lactosuria and glycosuria at different stages of pregnancy and puerperium.

TABLE IV—COMPARISON OF SUGAR EXCRETIONS IN PATIENTS WITH AND WITHOUT CHILDREN

—	Patients with no children	Patients with children	Distribution correction for children group
No of patients in group	29	29*	
No of patient attendances	321	322	
Percentage of patient attendances with lactosuria	61 1	42 6	+0 7
Percentage of patient attendances with glycosuria	26 1	17 7	+0 1

* Of these patients 20 had 1 child 7 had 2 children, 1 had 3, and 1 had 6

recorded as having been detected at the clinic in only 2 of the antenatal specimens of urine , our findings on the same specimens were 1625 green-1 reductions and 104 green 2 or heavier reductions At the clinic urine is tested for sugar by the Benedict test, but the quantities are not measured precisely, the tube is heated over a bunsen flame, and the result is recorded immediately

The results of the Benedict tests show a progressive rise in the percentage of positive tests as pregnancy proceeds Richardson and Bitter (1932) and Weiden (1948) found a uniform incidence throughout, but they examined fewer specimens

Chromatography Results

The results of the chromatographic analyses confirm the findings of Brock and Hubbard (1935) that lactosuria occurs not only during lactation but also in a large proportion of pregnant, and a small number of non-pregnant, women Our results also establish that lactosuria occurs in a few men taking a normal diet Lactosuria has previously been reported as occurring in men after ingestion of 10 g or more of pure lactose (Folin and Berglund 1922, Watkins 1928, Winter 1931), but the methods of identification were not entirely satisfactory

As indicated earlier, the finding of many workers that lactosuria in antenatal patients occurs either not at all or only towards the closing stages of pregnancy can be attributed to the use of methods of sugar identification which are of insufficient delicacy As can be seen from fig 2, the concentration of lactose present was almost always less than 100 mg per 100 ml , and indeed in most cases it was so low as to be near the limit of sensitivity of the method—i e , about 20 mg per 100 ml In the controls also the amount of lactose was minimal

TABLE V—COMPARISON OF SUGAR EXCRETIONS IN DIFFERENT AGE GROUPS

—	Patients aged 20–29	Patients aged 30–39	Distribution correction for group aged 30–39
No of patients in group	25*	25†	
No of patient attendances	284	260	
Percentage of patient attendances with lactosuria	46 1	46 8	+0 1
Percentage of patient attendances with glycosuria	11 6	25 6	+1 3

* Of these patients 7 were aged 20–24 years and 18 were 25–29
† Of these patients 17 were aged 30–34 years and 8 were 35–39

The sensitive and specific method adopted by Brock and Hubbard (1935) is alone satisfactory for the purpose of comparing our lactose results with those obtained by others Their method enabled as little as 10 mg per 100 ml to be determined quantitatively with great accuracy They found lactose in concentrations of 10–13 mg per 100 ml in 3 of 24 specimens from non pregnant women, 20–99 mg per 100 ml in 21 of 42 antenatal specimens of urine, and 20–399 mg per 100 ml in 9 of 11 postnatal specimens of urine These r closely resemble our own The fact that we found la in 9% of controls, when our method cannot detect than 17 mg of lactose per 100 ml , could be due to examining a larger number of specimens, to the incl of patients outside the age limits of 18–45 years, an dietary differences In some cases we found h concentrations of lactose than did Brock and Hub (1935) , this is certainly partly explained by our cor tion of the quantitative figures to a specific grav 1 020, which is probably higher than average norm

Our figures relating the incidence of lactosuria duration of pregnancy and puerperium establish tha frequency of lactose excretion increases with durati pregnancy between 12 and 35 weeks, and confirm finding of Watkins (1928) that the amount of lac excreted after delivery often increases to reach a p about the fourth day The findings of Brock Hubbard (1935), that lactosuria may not be present in pregnancy and may persist long after delivery, are confirmed

Apart from our finding that glycosuria occurs al 1½ times as frequently during pregnancy as in cont our results concerning glucose excretion do not con so closely to those of Brock and Hubbard (1935) found glucose in concentrations over 14 mg per 100 in 9 of 24 controls, in 32 of 42 antenatal specimen urine, and in 7 of 11 postnatal specimens of u Richardson and Bitter (1932), who used a fermenta method to detect glucose, also found this sugar l frequently , they found glucose in concentrations 14 mg per 100 ml in 31 of 50 antenatal speci urine and in 15 of 50 specimens of urine obtained o twelfth day after delivery The discrepancy betw our results and those of these American workers mu due to differences in diet In the case of the puerperal specimens of urine our finding so few case glycosuria is certainly partly explained by our obta these specimens while the patients were fasting confirm that glycosuria occurring early in pregnancy not always persist until term, a view originally forward by Williams and Wills (1928) but not substantiated by Richardson and Bitter (1932) or Weiden (

TABLE VI—COMPARISON OF SUGAR EXCRETIONS IN PATI WITH AND WITHOUT TOXÆMIA

—	Patients without toxæmia	Patients with toxæmia	Distrib correc for gro
No of patients in group	44	44	
No of patient attendances	488	498	
Percentage of patient attendances with lactosuria	47 1	47 8	-1
Percentage of patient attendances with glycosuria	22 9	20 7	-1

Relation of Benedict Results to Chromatography Findi

The significance of a positive Benedict test i considerable import to both patient and clinician T is no doubt that even strongly positive tests during puerperium may be normal and are due almost ex sively to lactose Unfortunately it is difficult to deter to what extent positive tests during pregnancy are to lactose or glucose, since glucuronate was f extremely often, with or without these sugars, occasionally fructose and pentoses were also fo Comparison of figs 1 and 2 certainly indicates tha the second half of pregnancy slight reductions are likely to be due to lactose than to glucose It ther seems that, where the Benedict test is made as descr above, slight reductions graded as green 1 may be considered as normal during pregnancy

LE VII—NUMBER OF BREAST FEEDERS AND NON BREAST FEEDERS PROVIDING POSTNATAL URINE SPECIMENS

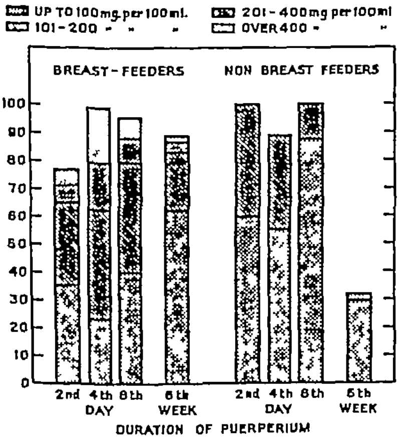
Duration of puerperium	* days	4 days	8 days	6 weeks
of breast feeders providing ine specimens	109	150	150	110
of non breast feeders pro ding urine specimens	5*	9	8	47

all these patients lactation was being suppressed with stilboestrol.

chanism of Production of Glycosuria and Lactosuria

here is abundant evidence that glycosuria during gnancy is at least partly explained by a lowering of renal threshold for glucose (Welz and Van Nest 1923 st 1925 Lawrence 1927, Williams and Wills 1928 iden 1948) Some workers maintain that a diminished ose tolerance also plays a part (Höst 1925 Williams Wills 1928), but more recently Weiden (1948) and kson (1952) have found that with few exceptions the od-sugar curve in uncomplicated pregnancy does not above normal limits Our finding that glycosuria more common among patients attending the after n clinic is compatible with these facts; thus, it is bably a reasonable assumption that patients attending the afternoon would have enjoyed a greater carbo rate intake just before their visit than those attending morning clinic The more frequent excretion of ose by patients in the older age group might be due glucose tolerance diminishing slightly with age; thus been demonstrated in males by Smith and Shock 49)

xcept during the puerperium there is less certainty ut the mechanism by which lactose comes to be reted in the urine There is good evidence that there o renal threshold for lactose (Winter 1932 Brock and bbard 1935) and it has been established by amputa of the udder in goats that breast tissue is the only rce of lactose during the puerperium (Porcher 1904) ollows that lactosuria must result either from synthesis actose in the mammary glands or from absorption of ose from the gut without prior splitting into glucose galactose The occurrence of spontaneous lactosuria h equal frequency in male and female control patients suggests that in these patients the source of the sugar is the gut. The experiments of Watkins (1928) and Winter (1931) with oral administration of lactose suggest that lactosuria may arise in this way Since lactosuria occurs much more often during pregnancy it is unlikely to be alimentary in origin at that time unless one postulates either a diminished lactase activity or alternatively a greatly augmented milk intake Pregnant women in this country are given a free pint of milk which contains 26 g of lactose but this extra milk is unlikely to explain spontaneous lactosuria since Watkins (1928) has shown that tolerance to oral lactose during pregnancy is two or three times greater than normal On the other hand the progressive development and secretory activity of the breasts during pregnancy could explain the frequent occurrence of lactosuria and its greater incidence in the later months. On balance a mammary origin seems more likely Our finding that lactosuria occurred slightly more often in patients attending the afternoon clinic might indicate a diurnal variation in lactose synthesis The finding that lactosuria occurs less often in multiparæ is interesting it could be explained on the basis that their breasts having previously undergone complete development can more readily accommodate the small volume of secretion without the pressure rising within the alveoli leading to reabsorption of lactose Thus Watkins (1928) postulated that lactosuria during lactation resulted from milk production exceeding milk removal The fact that we often found lactosuria in those in whom lactation was being suppressed supports this hypothesis



3—Incidence of lactosuria in breast-feeders and in non-breast-eders. The number of patients providing specimens is shown in ble vII.

Summary

The excretion of sugars in the urine during pregnancy and the puerperium has been reinvestigated by paper partition chromatography Results are presented of both qualitative Benedict tests and chromatographic analyses on single specimens of urine from 372 control patients and on 2373 antenatal and 657 postnatal specimens of urine from 245 pregnant women

With a critical technique a very high incidence of Benedict reductions was found during pregnancy (72 9%) and after delivery (87 8%) Where this test is done carefully reduction during pregnancy is often due to lactose

Lactosuria occurs in male as well as non pregnant female patients on normal diet. Lactose usually traces was detected in the urine of 9% of controls of either sex; this is probably alimentary in origin.

Lactosuria is common during pregnancy, occurring about twice as often as glycosuria Lactose usually in small amounts was found at 51% of all antenatal attendances being detected at some time in 94% of patients attending the clinic regularly Glucose was found at 24% of antenatal attendances but 33% of regular attenders never excreted detectable quantities of it

Antenatal lactosuria increases in incidence as pregnancy advances was found more often in the afternoon and more commonly in primigravidæ

Antenatal glycosuria was found more often in the afternoon and more frequently in older patients.

The frequent excretion of considerable quantities of lactose during the puerperium is confirmed and pregnancy glycosuria was found to disappear rapidly after delivery

In pregnancy glycosuria is probably due to a low renal threshold for glucose, and lactosuria to escape of lactose formed in the mammary glands

Glucuronate was found very often in the antenatal specimens of urine and traces of pentoses and fructose were found in a few cases.

A new spray reagent for showing up sugars on paper chromatograms is described.

We thank Prof W C W Nixon for permitting us to obtain urine from the obstetric patients and for giving us access to their clinical records, the nurses in the Obstetric Hospital for their great help with the collection of the urine, Mr V K Asta for the standard colour charts and the diagrams, and Miss D Bryant for technical assistance Work included here was done during the tenure by one of us (P de M) of a grant from the Rockefeller Research Fund of University College Hospital Medical School

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IMPALEMENT OF THE RECTUM

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Injury of the rectum is relatively uncommon in civilian life, and the published reports are of small series of individual cases and collective reviews These deal mainly with impalement injuries caused by the patient falling or sitting on an upright article, the configuration of the thighs and buttocks causing the instrument in many cases to enter the anus

Van Hook (1896), reviewing the published cases, pointed out that the injury occurred in males in 75% of cases, falling on to a pitch-fork being the common mode of injury Habbegger (1912) reported a mortality of 26 8% in 179 cases, rising to 78 5% when the peritoneal cavity and abdominal viscera were involved This indicates that the lesion is potentially serious, but the use of antibiotics has greatly improved the prognosis

Types of Injury

There are two main varieties in the first the offending object enters the anal canal directly, in the second it enters the rectum after passing through the buttock or the perineum When it enters the anal canal directly, the laceration of the rectum is commonly situated on the anterior wall 2 or 3 in from the anus The extent of the injury naturally depends on the force of penetration It may be a superficial laceration of the rectal mucosa, or it may penetrate the bowel wall and enter the pelvic cellular tissue or reach the peritoneal cavity or the bladder There may be no outward evidence of the injury on examination of the anal region, and this may cause some delay in the diagnosis of a rectal wound

The injury of the buttock opens up the ischior fossa, a fat containing space particularly liable infection An abscess forms in the loose parar tissues quickly and may be overlooked In this situa rapid resolution is unusual and may lead to the format of chronic abscesses or to fistulæ Seybold et al. (19 reporting seven cases seen in the Mayo Clinic betw 1910 and 1939, point out that only one patient wa hospital for less than thirty days, the remainder b detained longer because of infection The preventi such infection should be possible with early diagn and adequate treatment

Injury of the perineum may include laceration of urethra, here again early treatment will avoid ser complications and later development of a stricture.

Diagnosis

Examination of the patients in the more serious inju reveals usually only a slight degree of shock, the they may be in considerable pain

Local examination of buttock and perineum may s slight bruising of the anus if the article has entered t anal canal Lacerations of the buttock will be evid and should be inspected in a good light, and an atter should be made to determine the direction of entr the offending article Digital examination of the rect may not always reveal a wound of the rectal wall, t only indication of this may be blood on the exa finger

Abdominal examination in cases of peritoneal penet tion will show lower abdominal tenderness and mu guarding in the early stages Later, well-marked rig will develop and the bowel sounds will usually absent

The *urine* should be examined at the earliest opp tunity, the patient being catheterised if unable to p urine normally The presence of blood indicates d to the bladder, cystoscopy would then be indicated determine the site and extent of the damage

Proctoscopy is essential and will reveal the lacera *in most cases* The mild *case* will *only* show bruising the rectal wall, penetration into the peritoneal cav cannot be diagnosed with certainty by this examinat Sigmoidoscopy with the introduction of air is con indicated

Radiography—The abdomen should be X rayed every case Involvement of the pararectal tissues c be shown by the presence of air outside the rectal w Peritoneal penetration will be shown by the presence a small amount of air under the diaphragm in the e position Dilatation of loops of the small intestine, d to the early onset of peritonitis, will be present in ab six hours Free fluid between bowel loops will be ev in the later stages of peritonitis

Treatment

Shock will be treated in the usual manner, but morph should be withheld until a definite decision has been m regarding peritoneal involvement

Wounds of the buttock should be fully explored u general anæsthesia and surgical toilet done The wou are left open and allowed to granulate

A wound of the perineum is explored, special attent being paid to the urethra Damage to this struct should be repaired by suture over a catheter possible Suprapubic drainage of the bladder is th indicated

Laparotomy is indicated in all cases of perito involvement, and should be done in any doubtful c Even in early cases well-marked hyperæmia of the bo wall and thin purulent exudate are found With t patient in the Trendelenburg position the small intes is lifted out of the pelvis and examined for lacerat The wound in the rectum is next exposed and su-layers. Drainage of the pelvis, through the lower end the incision, is necessary James (1940) makes no empt to suture the rectal wall but covers the laceration th a peritoneal flap It is considered safer to suture e rectum if possible, to prevent continued infection of e pararectal tissues. The bladder is next examined; a wound is found it should be repaired with two layers sutures and suprapubic drainage should be instituted *e remainder of the bowel is next inspected for tears* tention should be given to the mesentery for any scular injuries a slowly developing hæmatoma should dealt with because it may later devitalise an area of wel. James (1940) reports a complete tear of the mesen ry of the sigmoid colon but this did not require resection the bowel Laceration of the duodenum has been ported on one occasion. The presence of retained reign bodies should be investigated.

Colostomy is indicated in the following circumstances) a large laceration of the rectum which is difficult to ose (2) a wound involving the rectum and buttock, an endeavour to lessen the infection in this region; d (3) severe damage involving rectum and bladder e colostomy can be closed when the rectal and buttock ounds are healed. This takes from three to six weeks cording to the severity of the injury

The patient should receive antitetanic and anti gas ngrene serum Phthalylsulphathiazole 10 g daily is ven by the mouth Penicillin or aureomycin in adequate ses is also given If peritonitis is well developed travenous fluid should be given and gastric suction arted early to combat paralytic ileus.

Case-reports

Case 1 —A schoolboy aged 14 was admitted to Bridgend eneral Hospital at 12.30 P.M on May 2 1950 An hour fore admission while jumping over cricket stumps in the aying field he fell and a stump entered his anus through s trousers He complained of severe spasmodic suprapubic in and nausea. He passed a bloodstained stool but could t pass urine

Examination showed pallor, slight cyanosis, pulse rate 108 d temperature 98 8°F Generalised abdominal rigidity was esent with much tenderness in the lower quadrants. The adder was not palpable The anus had a small abrasion teriorly with some blood coming from the rectum.

At operation three hours after injury proctoscopy showed perforating wound 1 in. long on the anterior wall of the ctum and about 2 in. from the anus. The rectum was cleaned t and a tube inserted Cystoscopy showed a normal bladder parotomy revealed early peritonitis with a retroperitoneal ematoma on the left side of the pelvis. There was a wound in. long in the rectum just above the peritoneal reflexion his was sutured and covered with peritoneum A small ceration of the pelvic mesocolon was found and repaired A ainage tube was inserted in the pelvis. A left inguinal loop lostomy was done

Progress —On May 4 a mild paralytic ileus developed and as treated with intravenous fluids and by gastric suction roctoscopy on May 23 showed that the laceration had not ealed but complete healing had taken place by June 15 hen the colostomy was closed. The boy was discharged home June 29 when bowel action was normal

Case 2.—A man, aged 20 was admitted to Bridgend General ospital at 10 30 A M on June 2 1950 after falling 20 ft. om a ladder on to a wooden fence He was complaining of in in the buttocks His general condition was fair with ly slight shock.

Examination revealed an irregular laceration 3 in long on e left buttock about 3 in from the anus. Rectal examination vealed a laceration of the lateral wall of the rectum about /2 in from the anus. Abdominal examination showed no gidity or tenderness. Catheterisation produced 10 oz. of ormal urine Four hours later the patient complained of wer abdominal pain and examination showed lower abdo-inal tenderness and rigidity

At operation six hours after the injury the buttock wound as explored and excised Proctoscopy confirmed the laceration previously described and no damage to the sphincter muscles was seen no further lesion was found in the rectum Laparotomy revealed pelvic peritonitis with bloodstained purulent exudate A small laceration in the rectum found above the peritoneal reflexion was sutured; this laceration had not been found on proctoscopy Slight bruising of the pelvic colon and a small laceration of its mesentery were found No injury to the bladder was found A left inguinal loop colostomy was done and the pelvis was drained.

Progress—The patient received antitetanic anti gas-gangrene serum, penicillin, and sulphadiazine He developed mild paralytic ileus On July 18 proctoscopy showed the buttock wound, which was not healed, to be still communicating with the rectum This was healed by Aug 24 and the colostomy was closed on Aug 28 The patient was discharged home on Sept. 12, all wounds having healed. He was re-examined in six weeks and again two years later when he was symptom free There was a moderate amount of scarring in the buttock, and slight scarring was palpable in the rectum.

Case 3 —A boy aged 6 years, was admitted to the Cardiff Royal Infirmary on Aug 31 1952 after having fallen backwards on to a bamboo cane which pierced his trousers and entered his anus He vomited two hours later and complained of central abdominal pain. His bowels had acted twice before admission and the stool contained blood He passed urine normally

On examination his general condition was good slight abdominal tenderness was present, and bowel sounds were normal. Rectal examination revealed no laceration, no blood being present on the examining finger Slight bruising of the anal margin was present Radiography of the abdomen revealed no abnormality

Progress —The boy had a bowel action next day when a little blood was present. The abdominal pain and tenderness had gone. On Sept 2 a small lump was palpable in the anterior wall of the rectum. Proctoscopy on Sept 5 revealed a $^1/_2$ in. laceration of the anterior wall of the rectum 2 in. from the anus, with a slough in the base Bimanual palpation discovered an inflammatory mass about 1 in. in diameter anterior to the rectum The patient was treated with chloramphenicol and sulphathalidine Proctoscopy on Sept 17 showed that the laceration had now healed and the mass had disappeared He was discharged home on the following day Follow up examinations have shown the healing to be complete

Discussion

The main lesson to be learnt from these cases is that early treatment is essential in limiting infection Full examination and special investigations are necessary to determine the exact nature of the injury In case 2 where no abdominal tenderness was found on first examination radiography would probably have shown intraperitoneal gas and enabled the diagnosis of peritoneal penetration to have been made earlier In case 3 there did not appear to have been any peritoneal damage, though the patient complained of abdominal pain

It is essential in these cases to know whether the rectum is perforated and if so whether the peritoneum is involved

Colostomy is discussed by most workers and many do not advocate it strongly; but it seems advisable in most cases, even though it prolongs the period spent in hospital and entails a further operation for its closure (Powers and O'Meara *1939*, Siler and Bebb *1950*) Even with modern chemotherapy it was considered safer to do colostomy in two of these cases In the second case with perforation of the rectum through the buttock, it was essential to prevent spread of sepsis and later formation of fistulæ.

I am indebted to Dr Jeffery Jones Mr A. C. Lysaght, and Prof A. G Watkins for permission to publish these cases, and to Mr D J Harries for help in the preparation of this report

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EXERCISE TESTS DURING TREATMENT OF HYPERTENSION WITH HEXAMETHONIUM

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In the course of treatment of hypertension with hexamethonium I have observed that a few patients have appreciable subjective symptoms despite the fact that they have been given an apparently adequate dosage leading to a proper reduction of their blood-pressure in the upright position Such patients feel well at rest and when they walk about quietly, but feel dizzy on slight exertion and have to stand still, sit down, or even lie down

One explanation might be that, in these patients, hexamethonium did not prevent a considerable rise in blood pressure on exertion, but it was striking that the symptoms might also appear in patients who had not been troubled, before treatment, by pronounced symptoms of hypertension caused by exercise

It therefore occurred to me that the symptoms determined by exercise in such patients might be due to a fall in the blood pressure under treatment with hexamethonium during exercise, instead of the usual rise

Hitherto only a few reports have been published on blood-pressure during exercise under treatment with hexamethonium Hood et al (1952) state that under these conditions there is considerably less rise in the blood pressure than usual, but so far as I know a fall in the blood-pressure determined by exercise in the course of treatment with hexamethonium has not yet been reported

Investigation

I investigated the effects of exercise on patients treated with hexamethonium The procedure followed in these investigations, which were made with Krogh's bicycle ergometer, and the results of the investigations will be described in detail elsewhere Here mention will only be made of the importance of the exercise tests in finding the proper dosage of hexamethonium

The blood-pressure is measured with the patient erect, and a combined oral and hypodermic administration of hexamethonium, or of hexamethonium in polyvinyl pyrrolidone with the longer-lasting effect, has been used (Smirk 1952, Ronnov-Jessen and Bech 1953, Ronnov Jessen 1953) Exercise tests will be required only in the cases in which the adjustment of the patient to the dose is beset with the difficulties mentioned above

Illustrative Case-records

Case 1 —A fisherman, aged 57, had an attack of violent hypertensive encephalopathy, since when he had had increasing dyspnœa on exertion for a couple of months For this reason he could walk only about 50 yards at a time when admitted

Treatment —Since his condition remained unchanged after a fortnight's stay in hospital and he was still hypertensive, treatment with hexamethonium was begun

Progress —During the next few months his condition improved considerably, and he could ride a bicycle 3–6 miles without being tired [illegible] the day his systolic blood pressure was 110–150 mm Hg in the u posture, and his general health was excellent Afte months' treatment he began to complain of dizzines oppression in the precordial area, even on moderate exe These symptoms were most pronounced during the first hours following the injections The blood pressure in upright posture had remained unchanged and satisfa

Exercise tests with Krogh's bicycle ergometer (fig 1) sh that, with a blood pressure of about 145/110 mm. Hg the patient sitting (corresponding to 125/95 mm. Hg in upright posture), the blood pressure fell considerably a sense of epigastric oppression developed when the exe amounted to 360 kilogramme metres (kg.m) per minute 2 minutes With an intensity of 540 kg.m per minute 1½ minutes the patient became pale and felt unwell dizzy, with precordial oppression and a fall in the blo pressure to 110/70 mm. Hg With a blood pressur 160/110 mm Hg with the patient sitting (correspon about 140/100 mm Hg in the upright posture) the fall much lower, and the patient had no complaints An at was therefore made to maintain a systolic blood pressur 140–160 mm Hg in the upright posture During the t weeks since then the patient has been feeling better and been much less troubled by his condition

Case 2 —A farmer, aged 55, with severe hyperten albuminuria, and pronounced retinal changes, had been a few months completely unfit for work, with severe att of hypertensive encephalopathy, dyspnœa on exertion, a attacks of stenocardia

Treatment and Progress —Hexamethonium therapy duced considerable subjective improvement and got rid of headache and dizziness, and the patient was feeling well a blood pressure of 150/100–200/120 mm Hg in the up posture compared to the former pressure of about 2 mm Hg When he was allowed to go for walks outside precincts of the hospital, however, he began to complain dizziness and general malaise when he walked rather quic especially during the first few hours after an injection.

Exercise tests (fig 2) showed that he could intensity of exercise of 540 kg m per minute for 2 minutes minute after a minute's rest without being troubled and a resulting moderate fall in the blood pressure when original pressure was about 200/120 mm Hg, but he collapsed doing the same amount of exercise when the blood pressure was about 180/105 mm Hg In this pat who had the same blood pressure in the sitting and upright postures, we therefore tried to keep the sy blood pressure 190–200 mm Hg During the twelve w since then the patient has been feeling well, though he is somewhat dizzy on too great exertion.

Discussion

The fall in the blood-pressure on exertion in th patients is presumably due to the effect of hexamethon

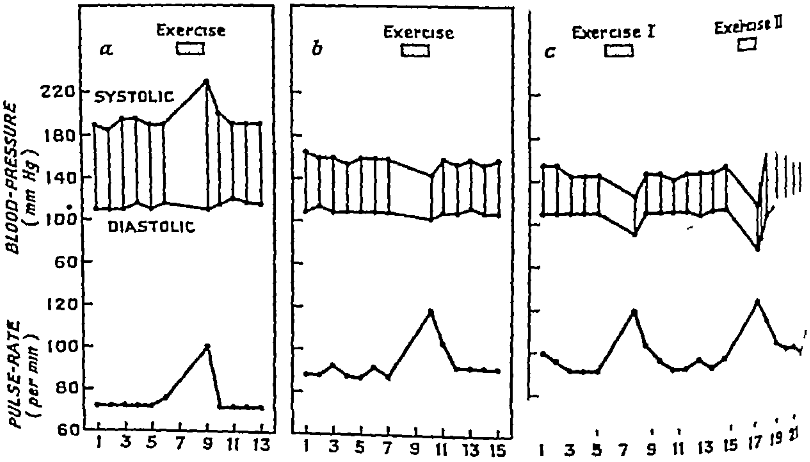
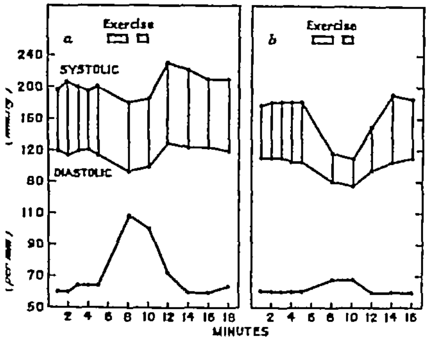


Fig 1—Changes in blood-pressure of case 1 during exercise (360 kg m per min for 2 min) a methonium in last 24 hr and patient had no complaint other than slight precordial b, 2 hr after hexamethonium bromide 100 mg in 25% polyvinylpyrrolidone hypodermically had no complaint after exercise c 1 hr after similar injection patient had precordial op after exercise 360 kg m per min for 2 min (I), and became pale and complained of dizziness, ma and precordial oppression after exercise 540 kg m. per min for 1½ min (II)



2—Changes in blood-pressure of case 2 during exercise (540 kg.m. er min. for 2 min. + 1 min. after a minute s rest) : a, 7 hr after podermic injection of hexamethonium bromide 230 mg in 25% olyvinylpyrrolidone patient had no complaint apart from fatigue legs after exercise; b 2 hr after similar injection patient became ale, felt dizzy and unwell and nearly collapsed.

the sympathetic, preventing the depletion of the blood pots in the course of exercise when the dose adminis ed is too large This means, in other words that there failure of the inflow into the right ventricle It appears case 2 (fig 2b) that there was only a slight increase in pulse rate during exercise when the effect of hexa thonium was vigorous whereas there was a normal rease in the pulse rate when the effect of hexameth ium was less pronounced (fig 2a) This is presumably e to the fact that in case 2 hexamethonium produced very effective block of the sympathetic nerves to the art. Generally a less pronounced blocking effect on the mpathetic nerves to the heart is seen

The importance of these observations is as follows

1) When the blood pressure in the course of treatment with xamethonium falls below a certain level some patients w during exercise an additional fall in the blood pressure h resulting hypotensive symptoms and presumably a risk thrombosis in the brain and the heart.

2) Patients like case 2 can presumably be protected to ne degree against stress on the circulation during exercise n though the reduction of the blood pressure obtained at t is rather slight There can hardly be any doubt that some es in which treatment has been abandoned have been of same type as case 2 These patients had such severe nplaints after a fairly slight reduction of blood pressure it it was wrongly believed that treatment would be of no

Conclusion

The exercise tests have shown that some patients whose od pressure had fallen to a reasonable level during atment with hexamethonium had an additional fall blood pressure during exercise with resulting hypo sive symptoms Such patients should have their od pressure adjusted so far as possible at a suitable her level, so that it fluctuates only slightly during ercise

In the treatment of hypertension with hexamethonium nerally the ideal would be to adjust the blood pressure that it shows only slight fluctuations during exercise. ere are presumably only a few patients in whom this incompatible with a more considerable reduction of blood pressure towards the normal in the upright sture

Summary

In most hypertensives the reduction of the blood ssure towards the normal in the upright posture is mpatible with only small fluctuations of blood essure during exercise but in some patients treated with hexamethonium the blood pressure falls considerably during exercise, with resulting hypotensive symptoms

By means of exercise tests these patients can have their blood pressure adjusted to a level which allows them to exercise without any appreciable fall in the blood pressure

A few patients treated with hexamethonium develop symptoms of hypotension during exercise even though the blood pressure in the upright posture has been only comparatively slightly reduced. If this is recognised and a somewhat slighter reduction than usual is therefore attempted these patients may nevertheless be beneficially treated with hexamethonium

Messrs May & Baker Ltd supplied the hexamethonium compounds.

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RESPIRATION PUMP FOR POLIOMYELITIS

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The use of positive pressure artificial respiration through a cuffed tracheotomy tube has been advocated by Lassen (1953) for some cases of poliomyelitis. The indications for using this method are not yet fully determined but it seems desirable that poliomyelitis units should be prepared to establish this type of artificial respiration when other methods prove inadequate

The machines described here have been designed to supply the air and/or oxygen required at any desired pressure, rate, and volume and have both been shown to operate satisfactorily for 4 weeks in a case of poliomyelitis in which there was extreme spinal and bulbar paralysis after this period natural respiration returned

It should of course be emphasised that, as Lassen pointed out, very careful supervision by anæsthetists is required for these cases whatever system may be used for delivering the necessary air or oxygen

The two pumps described here have these factors in common :

(1) The pressure under which air is delivered to the patient is obtained by weights pressing downwards on the top of the bellows or piston so that no accidental circumstance can increase the pressure beyond the maximum attributable to the weight selected

(2) The pressure can be varied by varying the weight

(3) The volume of air delivered at each stroke can be adjusted by controlling the length of travel of the piston or bellows top

(4) The respiration rate can be adjusted by altering the speed of the driving or regulating motors

Pump A (fig 1) is driven by an electric motor pump B (fig 2) by vacuum The suction system provided in the wards and theatres of this hospital provides a negative pressure of 10–20 in Hg and was found to be a convenient and satisfactory source of vacuum to operate pump B

PUMP A

The motive power and speed regulation are provided by a universal motor with a built-in rheostat and reduction gearing giving an output of 60–200 r p.m The rotation is transmitted by a pinion to a large gear wheel, the speed reduction being about 1 : 8 Thus the maximum respiration-rate is 25 per min , the minimum usable speed is about 14 per min The air movement is obtained by the 'Oxford' inflating bellows (Macintosh 1953) The large gear rotates about a horizontal axis, and about $^3/_4$ in from its face is a vertical slideway, the centre of the gear being in the same plane as the centre line of the slideway A slipper mounted on this is provided at its upper end with a projecting fork which engages with the handle of the bellows The slipper carries near its lower edge on one side a horizontal fin projecting towards the gear On the gear is a rubber-tyred roller mounted with the eccentricity needed to give the desired length of movement to the slipper As the gear rotates, the roller, when it leaves its lowest position and starts moving upwards and to the side, passes under the horizontal fin of the slipper and, as its movement is continued, carries the slipper upwards with it until it has moved so far to the centre line again as to disengage itself from the fin

In the original form of the pump the slipper was then free to move downwards by gravity driving the top of the bellows with it This was found to give too long a time interval between the end of inspiration and the beginning of expiration, because the expiratory valve at the patient's end of the air delivery tube did not open until the slipper had started to rise again This difficulty has been got over by holding the slipper at its highest position with a spring-loaded catch until the catch is thrown out of action by the roller in its downward path The weight of the slipper is enough to give an air-pressure of about 14 cm H_2O Additional weights placed on the top of the projecting fork can bring it up to more than 20 cm The volume of air delivered is regulated by a movable stop which limits the downward travel of the slipper

PUMP B

The body of the pump consists of a brass cylinder clamped between upper and lower end-plates The lower plate carries the delivery nozzle and the inlet tube and valve There is a side nozzle on the inlet tube with a stopcock for introducing oxygen when required

The cylinder contains a heavy brass piston carrying the conventional leather cup facing downwards It is guided by a rod passing through a bearing in the upper plate Above the bearing the rod passes through a collar, to which it is fixed by grub screws This c limits the downward motion of the piston and ser a rest on which additional weights can be placed movement of the piston is regulated by a rotating driven by an electric gramophone motor Its can be varied between 14 and 24 r p.m by using centrifugal governor of the motor The valve in a bronze body with two pairs of nozzles on the opening from internal ports in the bore (A1 and and B1 and B2) The ports of each pair are one immediately above the other The valve has a cut in it, which when it comes to a pair of ports connects them One of each pair of ports (A1 and is connected by its associated n a length of tubing to the upper of the cylinder, and the two rem ports (A2 and B2) are connected tively to the suction mechanism and free air Thus, when the recess is A1 and A2, air is sucked from the part of the cylinder and the piston till it reaches its limit, which is set b adjustable stop A gas tap regu the speed at which the piston can The recess occupies about 120° of circumference of the valve, and a time after it has passed over A1 and it starts to connect B1 and B2 this happens, the pressure in the up part of the cylinder returns to atmosph and the piston consequently falls, expel air from the delivery nozzle Its ra fall depends on the resistance met with the expelled air and its weight It s times happens, both with pump B with pump A, that the resistance is great to allow the piston or bellows to reach its lower limit in the time avail

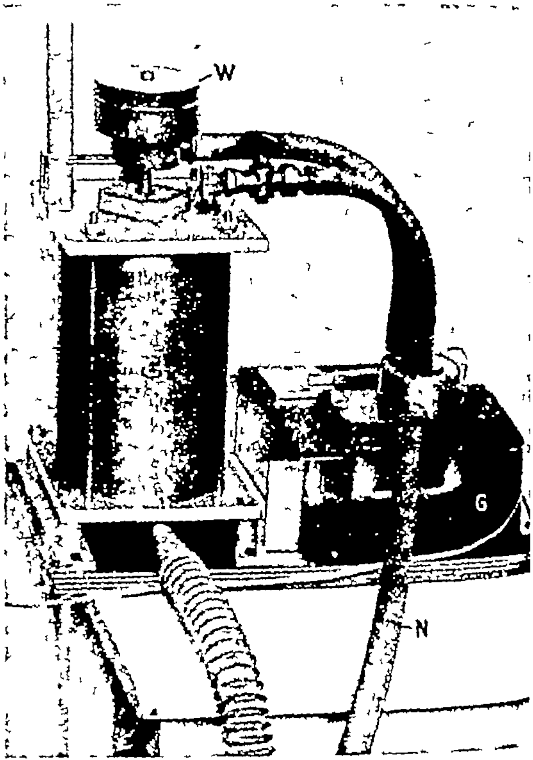

Fig 2—Pump B W, weight-operated piston in cylinder (C), delivery tube from hospital suction system ; G, gramophone operating valves.

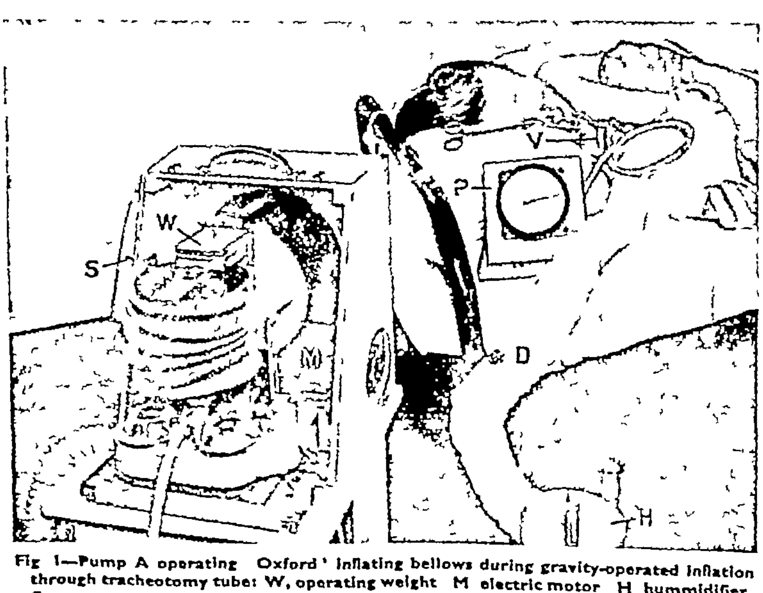

Fig 1—Pump A operating 'Oxford' inflating bellows during gravity-operated inflation through tracheotomy tube: W, operating weight M electric motor H hummidifier P pressure gauge ; D, lagged delivery tubing V, expiratory flutter valve (Stott) ; stop for volume control

is may be taken as a danger signal The exact position the piston and its actual range of motion are indicated a pointer attached to its rod which moves up and own a vertical scale rising from the upper plate whose ivisions represent amounts of 100 ml

A good method of controlling delivery of the appro riate proportion of oxygen and air by either of these umps is *provided by attaching an anæsthetic bag to* e air inlet and feeding into this bag the desired mixture f gases through an entrainment device

These initial designs, though capable of being improved, rovide a safe form of apparatus which is adjustable ot only for rate but also for pressure and volume

The pumps are manufactured with improvements by essrs H. G East & Co. Longworth Road Oxford and e named "Radcliffe Respiration Pumps A and B The xpiration valve used was the flutter valve designed by Dr D Stott and manufactured by Messrs. Owen Mumford, reen Place, Abingdon Road, Oxford With this in use the se of the expiratory valve on the inflating bellows must be moved. We are indebted especially to Dr A Crampton mith and Dr J M K. Spalding for supervising the use of ese machines

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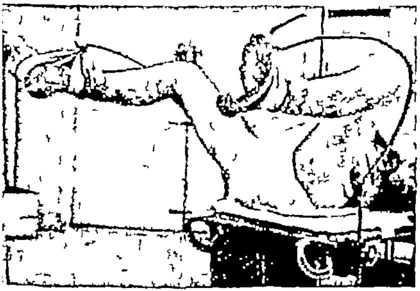
New Inventions

LEG SUPPORTS FOR CYSTOSCOPY AND PERURETHRAL RESECTION

In cystoscopy the position of the patient's legs is a tter of some importance; it affects both the comfort the patient and the convenience of the surgeon. It tters even more in perurethral resection and other doscopic operations. The leg supports should hold the s flexed not more acutely than a right angle and ould not come between the surgeon's head and the tient's thighs, thus allowing the fullest range of vement of the endoscope as in excavating the lateral es of the prostate or in catheterising an awkwardly uated ureteric orifice. The perineum should be flush th the end of the table and it is an advantage to have feet high enough to be out of the way A proper stoscopy table may meet all these requirements, but is not always convenient to use it in a theatre which is t devoted entirely to urological work.



The supports illustrated here hold the legs in the quired position They are a variant of the ordinary ithotomy supports and can be fitted to any standard eration table. They were made by the engineer's staff the hospital and are of stainless steel The iron protopes were in all important respects satisfactory but did t look smart enough to win general approval in the atre.

North Middlesex Hospital
London

B H PAGE
M.A., M.CHIR. Camb., F.R C S

Reviews of Books

The Spinal Cord

A Ciba Foundation Symposium Editors: J L MALCOLM M.B., D.MED.SC; J A. B GRAY M.A M.B Editor for the Ciba Foundation: G E W WOSTENHOLME O.B.E., M A., M.B assisted by JESSIE S FREEMAN M.B., D.P.H. London: J & A Churchill 1953 *Pp* 300 30*s*

In introducing the discussions of which this publication is the printed record Prof G L. Brown indicated that the symposium had been limited to the spinal cord in order to avoid the danger that the members might find with them 'people whose language we could not understand We felt that if we stopped at the medulla oblongata everybody would understand everybody else' From this arbitrarily narrowed territory there is but a single geographical departure—a contribution by Lorente de No on the conduction of impulses on the neurones of the oculomotor nucleus It must not be imagined, however, that this volume is a simple account of the present state of knowledge of the function and structure of the spinal cord, a Rattiganesque 'Reflexes without Tears, for to this anatomically limited field have been applied all the special devices of the electrical, pharmacological and anatomical worlds Two of the early sections deal with the anatomical organisation of motor cells in the spinal cord of sheep and cats, but the motif in most of the contributions is biochemical or electrical. The contributors are internationally famous in neurophysiology: Eccles, Lorente de No Laporte, Skoglund Matthews Adrian, Liddell Whitteridge and Young—to mention only a few In spite of the complexity of the work reported the information contained in the articles and the points raised in the subsequent discussions are of great interest not only to neurophysiologists but to clinical researchers and clinicians in neurology generally The articles dealing with the effects of various drugs on monosynaptic and polysynaptic reflexes are particularly interesting in relation to recent attempts to relieve clinical spasticity The printing is clear and easily readable, and the diagrams well set out and understandable—respects in which this record of a symposium differs from some others

Fifty Years of Medicine

Lord HORDER G C V O, M.D F R.C.P London Duckworth. 1953 Pp 70 5*s*

This book is an expanded version of the three Harben lectures delivered in December 1952 at the Royal Institute of Public Health and Hygiene The first lecture entitled The Birth of Scientific Medicine describes the progress made by medicine during the last half century The second, Medicine Enlarges its Boundaries, discusses, among other things, nutrition, physical medicine, industrial medicine and nursing The third on The Present and the Future contains a full blooded attack on the National Health Service Act and the Minister responsible, and tackles the problems of noise smoke cremation and hygiene in time of war—problems on which the author has himself done a great deal to arouse and guide professional and public opinion. Whether one agrees or disagrees he is always interesting and frustrated medical men will get full value from the seven pages dealing with medicine and the State

Synovial Fluid Changes in Joint Disease

MARIAN W ROPES M.D., associate physician; WALTER BAUER, M.D., chief of medical services, Massachusetts General Hospital Boston Cambridge Mass.: Harvard University Press. London Oxford University Press 1953 Pp 150 25*s*

This is a first-class piece of work. The publisher's note calls it a distinguished definitive study of joint fluid in health and disease.' This is no exaggeration; it is a painstaking evaluation of the results of some 1500 specimens of synovial fluid in various diseases and is presented with obvious fairness. The authors have had the same difficulty as other workers in this field in obtaining normal synovial fluid to act as a basis for comparison but this is really an interim report on their studies, which extend back over the last twenty years, and there is admittedly still a great deal to discover

From their already massive data they have been able to divide joint disease into two major groups—a "traumatic" group (which includes degenerative arthritis osteochondritis dissecans, and Charcot's joints) and an "infectious" group (which includes rheumatoid arthritis and tuberculosis) By examination of the synovial fluid, these two groups can be fairly reliably differentiated With the knowledge they put at our disposal the diagnosis of the "observation knee" and other obscure effusions into joints is going to be facilitated Within the groups, the findings in each disease are admittedly not so helpful in diagnosis, though in many instances they can be strongly suggestive

This book, which is one for the specialist, expresses the results of a major piece of planned research There is no padding but so far as is possible with such concentrated material the facts are presented in a readable way

Diseases of the Ear, Nose and Throat

A Textbook of Clinical and Laboratory Procedures GEORGES PORTMANN, M D, professor of otorhinolaryngology, University of Bordeaux Baltimore Williams & Wilkins London Baillière, Tindall, & Cox 1951 Pp 728 £7 10*s*

Professor Portmann is a prolific author of books and contributor to journals The quantity of his published work is astonishing, but what is even more astonishing is its quality and diversity All these attributes are illustrated in this book, which appeared two years ago It comes as a surprise to learn that so many investigations of such different kinds are possible, but it would test the energies even of the author to use all of them, and most readers would welcome more critical guidance in their selection. As in all French textbooks the anatomical sections are particularly good, but the ear, nose, and throat specialist in this country rarely attempts also to be a radiologist, and the long descriptions with numerous illustrations of radiographic technique seem out of place Nevertheless, the better understanding of the methods employed, which a study of these descriptions will inevitably induce, must lead to an improvement in interpretation Tests of function of the cochlea and vestibular apparatus are exceptionally well described and illustrated, but again there is no reliable guidance on which tests to select The American translators have adequately conveyed the fluent and emphatic manner of the original

Functional and Surgical Anatomy of the Hand

EMANUEL B KAPLAN, M D, F.A C S, assistant professor of anatomy, Columbia University, New York Philadelphia and London. J B Lippincott 1953 Pp 288 80*s*

THIS scholarly work, written by a man who is both a practical anatomist and a practising orthopædic surgeon, is not intended to be encyclopædic Nevertheless the lymphatic system is the only aspect of the subject which is treated really briefly The illustrations—especially the diagrams demonstrating the action of the various muscles in movements of the fingers—are particularly good Much of the work is original, and in consequence the description of the mid-palmar fascia and the various septa attached to it differs from accepted teaching in several respects, being of special interest in connection with Dupuytren's contracture

A few tables might have been helpful, particularly in the listing of possible variations The wording is not always clear, and there are some minor errors—such as reference to the phalanx when the metacarpal is meant, and vice versa The index is good, and the value of the carefully chosen bibliography is greatly enhanced by the brief notes which the author has added under many of the more important listed works, calling attention to the special significance of each

The book can be highly commended to all interested in the subject.

Long-term Diabetes

KNUD LUNDBÆK, M D, Copenhagen, lecturer in internal medicine Aarhus University Copenhagen Ejnar Munksgaard 1953 Pp 197 Cr 32

THIS book is described on the title page as giving the clinical picture of diabetes mellitus of 15–25 years' duration, with a follow-up of a regional series of cases A [illegible] 165 living patients in the series were followed up, and information was obtained on the 69 who had by the time the series had been collected The pictur the incidence of complications and their correlat may therefore be considered reliable for this par Denmark, even though some of the information had be obtained retrospectively A number of interest points emerge Thus two-thirds of the diabetics 60–70 years had heart-disease, and diabetic retin was present in 77% In spite of this, only 3% of t series were disabled by poor eyesight, and the incide of retinopathy did not increase after 15 years' durat of diabetes The author also comes to the conclusion that there is nothing to suggest that catar is a long-term diabetic manifestation In discussing controversial question of the relation of diabetic cont to the incidence of complications, he feels safe in c cluding only that retinopathy was less common in th with good control, but the range of control in the does not appear to have been very extensive or easy decide The monograph is valuable not only for t detailed information it contains but for the review published work

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Pitkin's Conduction Anesthesia (2nd ed Philadelp and London J B Lippincott 1953 Pp 1005 19 The American surgeon George Pitkin was a pioneer of l and block anæsthesia during the first part of this when the results of general anæsthesia were harder on patient than those of the surgery itself Conduction an thesia was his hobby, and he spent a great part of hi compiling notes and having illustrations made of suc techniques He died in 1943, three years before the edition of this volume—which is based in part on his o work—was published, and one year after the first paper written on the use of curare in clinical anæsthesia advent of the muscle relaxants has revolutionised ge anæsthesia to such an extent that the need for local or b methods has steadily diminished Good general anæst is now less exacting, and is usually followed by fewer comp tions, than are some forms of purely local anæsthesia there is a field of application for local techniques in diag and therapeutics

This book is the standard work of reference for all type local anæsthesia It is encyclopædic, containing des anatomy, pharmacology of drugs, full and liberally illustr descriptions of all techniques, and chapters on refrigera anæsthesia and on complications In this edition the ed (Dr James L Southworth, Prof Robert A. Hingson, Dr Winifred M. Pitkin) have successfully revised rearranged parts of the text to bring them up to date in light of recent knowledge Many new illustrations, an considerable amount of information concerning the co continuous extradural and segmental spinal anæsthe have been added

A Textbook of Medical Psychology (London Hog 1952 Pp 352 30*s*)—The tenth edition of Prof E Kretschmer's well known text (reviewed in THE LAN 1951, i, 894) appeared in 1950, with additions based on physiological research of W R Hess, and an expansion of section dealing with psychotherapy Dr E B Straus again rendered a service by providing a faithful transla which *is, on* the whole, clearer and more readable than original. The longer sentences are broken up, the abst nouns are made more concrete, and it is only rarely cloudy or compound terms, so easily accepted in Ger prove too much for him and he either invents a neolo such as "morphopoiesis," or takes refuge in literal transla Professor Kretschmer's disregard of work published languages other than German does not lessen the usefu of this book as a handy guide to large areas of Ger psychiatry, now rather regrettably neglected outside Germ

Guide to Human Parasitology for Medical **tioners** (5*th* ed London H K Lewis. 1953 Pp 25*s*)—Blacklock and Southwell's well known *Guide* maintained its popularity since the appearance of the fir edition in 1940 Now it has been brought up to date Prof T H Davey, and large sections of it, notably t malaria, have been rewritten in a clear, concise, and ac manner The three new coloured plates are all good, espec the one which depicts blood parasites in thick film prep tions, and draws attention forcibly to the most als artefacts This work remains unsurpassed in clarity judgment as a textbook for students and technicians, a groundwork for sincere practitioners of tropical medi

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THE LANCET

LONDON SATURDAY, OCT 3 1953

Mitral Stenosis

N the past few years much has been learnt about ral valve disease, but many problems are still olved The published results of mitral valvotomy encouraging with 60–80% of patients greatly proved but the mortality rate lies between 5% l 10%[1–3] The number of patients who die, or are improved, as a result of the operation might be *uced by better selection of cases Such selection* often difficult, since it is not always possible to dict whether a valve will be amenable to satis tory valvotomy, or whether other factors may vent a successful outcome

The great diagnostic difficulty is in detecting the ve which is incompetent as well as narrowed Pure greatly predominant, mitral incompetence can ially be detected readily enough by physical and liographic examination[4] but when mitral incompe- ice is associated with significant stenosis diagnosis y be much more difficult Any or all of the follow signs, in association with those of mitral stenosis uld arouse suspicion an apical systolic murmur of re than moderate (grade III) intensity, a soft first art sound and opening snap of the mitral valve, t ventricular enlargement, cardiographic signs of reased left ventricular dominance, and a very large t auricle on fluoroscopy The pulse is full,[2] rather an of small volume as in pure severe mitral stenosis ere are many further methods of assessing the degree mitral incompetence—notably observation of the m of the pulmonary capillary venous pulse by dging the cardiac catheter in a small branch of the lmonary artery[5 6] A large positive wave in ventri lar systole suggests incompetence[6 7] Although ere have been contrary reports,[8 9] *there is evidence* at the pulmonary capillary venous pulse reflects ssure changes in the left auricle[9 10], but a pattern nstant enough to be diagnostic of mitral incompe ice has not so far been agreed on, and similar curves y be found both with predominant mitral stenosis d with predominant mitral incompetence[11] The ophageal auricular pulse tracing and the electro- mogram have not proved helpful[12] while systolic pansion of the left auricle on fluoroscopy, although esent in pure incompetence[4] is also often seen in tral stenosis.[2 12] A loud systolic murmur at the ex *is probably the most important single sign of* tral incompetence[13] it may occasionally be sent in stenosis,[13] but in this event the first sound usually loud and the opening snap of the mitral valve clear[2] Careful clinical and radiological examination remains the most satisfactory method of diagnosing mitral incompetence Slight incompetence is no bar to operation, and may be reduced by successful valvotomy, but in the presence of pronounced incompetence valvotomy is useless Attempts to improve the function of incompetent valves by pericardial grafts and slings[3 14] have not yet proved wholly successful and until we have a reliable operation for mitral incompetence the condition of the mitral valve must be very carefully assessed before valvotomy is undertaken

In severe mitral stenosis the pulmonary vascular resistance is almost invariably increased and high *levels of pulmonary arterial pressure are commonly* recorded There is little doubt that both functional[15–18] and organic[19 20] narrowing of the smaller pulmonary arteries occurs and may be proportional to the degree of pulmonary hypertension[21] According to Lewis et al.,[22] when the area of the mitral valve (calculated by the formula of Gorlin and Gorlin[23]) is 1·0 sq cm or less and the pulmonary venous pressure rises to levels close to the colloid osmotic pressure of the plasma, narrowing of the smaller pulmonary arteries protects the pulmonary capillaries from the onslaught of the hypertrophied right ventricle By contrast, McGregor et al.[24] found that inhalation of oxygen produced a fall in pulmonary arterial pressure in 13 patients with increased pulmonary vascular resistance and they suggested that constriction of the pulmonary arterioles might be the result of anoxia secondary to pulmonary congestion and œdema rather than a protective change induced by pulmonary venous hypertension. The exact mechanism is still undecided, but pulmonary hypertension is an indication for operation,[1 2] and often a *fall* in pressure follows successful valvotomy[1 25] Low grade active rheumatic carditis, which may be very difficult to detect, may militate against success Valvotomy obviously cannot be considered in the presence of *acute carditis, but vague joint pains* and a moderately increased erythrocyte-sedimentation rate or anti streptolysin titre may have to be ignored when urgent symptoms of mitral stenosis demand operative relief. Even in cases where there is no clinical evidence of active carditis, biopsy material taken from the left auricular appendix at operation shows changes suggesting active carditis in 30–50% of cases[26] but these stigmata are not incompatible with excellent operative results[3 24] Auricular fibrillation, while not a contra-indication to operation indicates added risk, partly because of possible embolism from the left *auricle during operation and partly because the* disease is likely to be at a later stage than in cases where there is no fibrillation.[1] Fibrillation develops

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after operation in some 30% of patients, and in half of these it becomes established despite attempts at conversion to sinus rhythm [1] Heavy calcification of the mitral valve is an unfavourable feature which may prevent adequate valvotomy [1]

The results of valvotomy are best in patients under the age of 40, with slight or moderate cardiac enlargement, pure tight mitral stenosis (usually with pulmonary hypertension), slight or absent valvular calcification, sinus rhythm, and no other valve lesion A large heart, auricular fibrillation, heavy valve calcification, or slight mitral incompetence do not contra indicate valvotomy but limit the improvement Severe aortic incompetence and predominant mitral incompetence are absolute contra-indications to mitral valvotomy Tricuspid lesions do not necessarily contra-indicate operation,[1] while the development of operations for the relief of aortic stenosis [27] may make simultaneous aortic and mitral valvotomy possible A history of systemic embolism is now usually regarded as an indication for operation rather than the reverse [3] Mitral valvotomy should be considered in any patient with progressive symptoms due to mitral stenosis, and is urgently indicated in the presence of attacks of paroxysmal dyspnœa at rest and pulmonary œdema, especially in pregnancy [1 2 28] Assessment of benefit from the operation at present depends mainly on improvement in, or disappearance of, symptoms, changes in the physical signs of mitral stenosis and pulmonary hypertension, diminution in heart size, and reversion of cardiographic signs of right ventricular hypertrophy Cardiac catheterisation may reveal a fall in pulmonary arterial pressure after operation, but postoperative catheterisation is not always practicable or desirable, and other objective tests of improvement, such as those of respiratory function [29] and exercise tolerance,[30] are required

Many questions have still to be answered Will the mitral valve become narrowed after valvotomy as a result of further attacks of rheumatic infection or fibrosis, how may low-grade active carditis be detected, how treated, and how prevented, what is the mechanism of dyspnœa and of the pulmonary vascular changes, and how can the degree of mitral incompetence be reliably detected before operation ?

Tuberculous Meningitis

FURTHER welcome evidence of the value of isoniazid in the treatment of tuberculous meningitis is described in our columns this week Dr FLETCHER estimated the isoniazid levels in the cerebrospinal fluid (C S F) in 15 patients with tuberculous meningitis by two chemical methods, and controlled the results by a biological method Despite the vagaries and difficulties of the chemical methods, he found that he was measuring active isoniazid With a daily dosage of 200 mg adequate bacteriostatic levels prevailed throughout the illness, thus confirming the biological findings of KLEE [31] and GEHRT [32] With a daily dosage of 10 mg per kg of body-weight (two or three times the former dosage) the C S F levels were significantly higher, but, while there was still no evidence of toxicity with these doses, FLETCHER suggests that little purpose is served by having very high le circulating isoniazid since these are not nec associated with higher therapeutic activity TORRES GOST reports on large series of p with tuberculous meningitis who received int cular streptomycin combined with oral and intr isoniazid He emphasises the great improvem the outlook since isoniazid was introduced his first 100 patients given a three month there were only 6 deaths Of the others, 6 under observation for 3–7 months after their ment, 34 of these had been discharged to their without relapse, while 27 were still in hospita 10 relapsing The relapses were mild and resp well to further treatment In 7 cases there mild paralytic sequelæ, but none involved disability TORRES-GOST remarks that supp of the acute phase does not necessarily impl manent cure, and it will be instructive to see follow-up of this series and compare it with the after streptomycin alone, as given by DEBRÉ [33] reported a survival-rate of just under 50%, most of the deaths in the first 6 months) an CAIRNS and SMITH [34] (survival-rate of 50–60% 18 months) It may seem, in view of FLE work, that intrathecal administration of iso may be unnecessary, but TORRES-GOST fou intolerance to the intrathecal injections, nor dif in giving them GEHRT [32] has shown, too, that thecal isoniazid does not cause an increase i C S F cell or protein content Dr ANDERSON a colleagues (p 691) obtained successful resul giving streptomycin intramuscularly and intrath for 1 or 4 weeks only and relying mainly on iso (10 mg per kg of body-weight daily for 16 w Although in 3 patients *out* of 7 the disease "advanced" on admission, they had no de (CLARK et al [35] reported 3 deaths among 10 pa with tuberculous meningitis treated with iso alone) ANDERSON et al chose comparable co from patients previously treated with streptom and showed that the temperature fell and the returned to normal more rapidly in the pa who were given isoniazid than in those treated streptomycin, in those given isoniazid the cl recovery was very rapid They point out tha patients were much happier with the smaller nu of intramuscular and intrathecal injections C et al [35] suggested that much of the intrathecal i ference could be avoided by giving isoniazid by and streptomycin by mouth and intramuscul These clinical results agree fully with the histolo findings of RITCHIE, TAYLOR, and DICK,[36] who n that the lesions of miliary tuberculosis and tuberc meningitis undergo resolution during treatment isoniazid, while with administration of streptom similar lesions become fibrosed, in patients tre with both agents, the isoniazid effect predominate

In deciding on the treatment of choice in tubercu meningitis, the possibility of giving only isoniazi mouth must be considered Its action is rapid effective, and its administration involves no unpleas

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ss The Medical Research Council,[37] however showed at a third of all patients with pulmonary tuberculosis ated with isoniazid alone developed resistant tiants in 3 months, and this figure was reduced 2% when streptomycin and isoniazid were used in mbination Possibly these figures apply only to open' lesions, with the "closed' lesions of iliary *tuberculosis and tuberculous meningitis* the k of resistance might be much smaller Even so, would seem desirable to use a combination of both, the expense of some unpleasantness to the patient the form of intramuscular streptomycin especially this does not impair the efficacy of the isoniazid [38, 39] nce sufficient isoniazid enters the C.S F after al administration to be bacteriostatic, intrathecal jections, using the non irritant isoniazid, may per ps be confined to very acute cases when lumbar ncture is being done for diagnostic purposes It mains to be seen how little streptomycin is needed prevent the development of strains resistant to ther drug We need now to know the results in a ries of patients treated with isoniazid by mouth ily and with streptomycin by intramuscular injec on every second or third day Variants resistant to her streptomycin [38] or isoniazid [39] may be present fore any treatment is given, in which event the use *p* aminosalicylic acid with the other drug may have be considered In this form of tuberculosis the m must be to get the lesions to resolve as completely possible, but it is unlikely that any treatment ll prove universally successful

The Death Sentence

EVERY year some dozen people are judicially hanged England and Wales and their deaths are often tended by much unwholesome public excitement [40] it this important effect of executions since it nnot be abolished without abolishing the penalty elf did not fall within the terms of reference of the yal Commission on Capital Punishment [41] The mbers of the commission were called to discuss ly ' whether liability under the criminal law in eat Britain to suffer the death penalty should limited or modified and if so to what extent and what means', and they were expressly told the continuance or discontinuance of capital ishment was not for them to consider [42]

In this country liability to suffer the death penalty is already considerably modified by the Royal prerogative of mercy Of 1210 murderers sentenced to death in the first fifty years of our century, 23 had their conviction quashed on appeal 47 were certified insane and 506 were reprieved In every case the Home Secretary had the task of reviewing all the *circumstances extenuating the crime—including those* which had not been brought into evidence at the trial—and of deciding whether he could conscientiously ask the Sovereign to exercise the prerogative It is a curious system throwing much responsibility on the Minister and his advisers, and causing a solemn judgment to be pronounced unnecessarily upon a large number of frightened people yet as the report puts it the system ' works well in the sense that it produces results generally regarded as broadly satisfactory —' Broadly satisfactory ' that is, within the law as it stands at present Similarly in so far as it is possible to manage an execution by hanging humanely for the victim, the methods applied in our prisons are humane in England and Wales the time elapsing between the summoning of the prisoner and the act of execution is 9–25 seconds—one of the most impressive facts in the report But of course no expedition in the final act can relieve the prisoner and his family of the mental anguish of the weeks following the sentence, with its alternating periods of hope and despair

Hanging itself is believed to be an immediate and painless death comparing favourably in these respects with electrocution and lethal gassing Members of the commission visited America in order to establish this and the report gives their sound reasons for believing it to be so Nevertheless judicial hanging is claimed to have a ' uniquely deterrent ' effect which—if it exists—must be due to the grim associations of the gallows Actually there is no clear evidence that it has such an effect and there is no particular reason why it should Murderers do not form a homogeneous group many of them act under sudden provocation and murder is their solitary act of criminal behaviour others are not of a type to be deterred by anything demanding an act of imagination. The commission sum up by saying

> there is no clear evidence in any of the figures we have examined that the abolition of capital punishment has led to an increase in the homicide rate or that its reintroduction has led to a fall

The idea of the ' uniquely deterrent ' effect however influences public opinion, and so does the desire for retribution which is used by some as an argument against the introduction of euthanasia.

Why should a man who has coshed an old woman" the plain man understandably asks get an easier death than most of us can expect in the course of nature ?' The commission, however, state plainly their approval of the principle of euthanasia ' if we could have been satisfied that executions could be carried out in this way quickly, painlessly and decently in all cases we should have recommended its adoption unanimously ' They were deterred, curiously enough by the difficulties put before them by medical witnesses who seem to have been more anxious to ensure that no doctor should take part in an execution than to give the problem detached consideration The commission do recommend, how

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Medical Research Council, *Ibid* Aug 1 1953 p. 217

Pyle, M. M. *Proc. Mayo Clinic*, 1947 22, 465

McDermott W Muschenheim, C., Clark, C. M. Elmendorf D F Jun., Cawthorn, W U *Trans. Ass. Amer Phycns*, 193* 65 May

Lancet 1953 i, 280

Royal Commission on Capital Punishment, 1949–53 *London: H.M. Stationery Office 1953 Pp 506 12s 6d*

The members were Sir ERNEST GOWERS (chairman) Sir ALEXANDER MAXWELL, formerly permanent under secretary to the Home Office Earl PEEL, who resigned in 1950; Sir WILLIAM JONES, formerly clerk of the peace for Denbighshire; Dame FLORENCE HANCOCK chief woman research officer of the Transport and General Workers Union; Mrs. E. D C CAMERON (Miss Elizabeth Bowen the novelist); Mr JOHN MANN convener of the Lanarkshire County Council; Mr N R FOX, Q.C. recorder of Bournemouth Mr HORACE MACDONALD member of the executive committee of the Working Men's College; Prof G A MONTGOMERY Q.C., professor of Scots law at Edinburgh Mr LEON RADZINOWICZ, director of the department of criminal science at Cambridge; and Dr ELIOT SLATER, physician in psychological medicine at the National Hospital for Nervous Diseases ever, that this question should be periodically examined, with a view to a change of system being proposed to Parliament We are fully of their opinion, for whatever risks there may be in substituting euthanasia for judicial hanging, there can be no doubt that such a change would relieve beyond measure the sufferings of the condemned man's family, and do much to diminish the morbid interest of the public We also warmly support their recommendation (unfortunately not unanimous) that the death penalty should not apply to anyone under 21, the accepted age of adult responsibility

The outstanding defect of the law of murder is that it provides a single punishment for a crime varying widely in culpability fifty cases reviewed by the commission, in an appendix, show vividly how impossible it is to speak of "murderers as a class" We, as doctors, wish to feel confident that the death penalty does not befall any patient who, because of mental illness or abnormality, kills another person, and in recent years our concepts of mental illness and abnormality have so widened as to affect the legal definitions set out in the McNaughten rules The commission suggest that the rules might be extended to cover the fact that in some cases the accused, though he may know the nature of his act, and know that it is wrong, may be incapable of preventing himself from committing it They think it would be even better, however, to abrogate the McNaughten rules and leave the jury to determine whether at the time of the crime the accused was suffering from disease of the mind or mental deficiency to such a degree that he ought not to be held responsible This would take account of emotionally disturbed patients, including many guilty of sexual crimes, and of other abnormal people, including those of psychopathic personality, but of course it is difficult to know how the change would work out in practice—some juries perhaps being ready to accept psychological explanations while others were not It is disappointing, in this connection, that the commission specifically do *not* recommend a change of procedure which many of us have long thought desirable, and not only in murder cases—namely, the appointment of expert medical witnesses by the court rather than by the prosecution or the defence This, they say, would mean a fundamental change in the procedure of the courts and would have repercussions beyond the field of their inquiry

They do, however, propose that in England and Wales the mental state of every prisoner charged with murder should be examined by two doctors, of whom one at least should be a psychiatrist of standing who is not a member of the prison service, and the other usually an experienced member of that service The judge, in both England and Scotland, should be given the power, they think, to raise the issue of insanity, to call relevant evidence, and to put the issue to the jury, if he has reason to believe that the accused may have been insane at the time of the offence, and that the trial of this issue would be in the interests of justice, and they urge the immediate need for the establishment of an institution for the detention and treatment of psychopaths and other prisoners who are mentally abnormal though not insane, and for research into the problems of psychopathic [illegible]lity.

Much comment has already been excited by the commission's revolutionary suggestion that the j having in the first part of the trial decided the question of guilt, should then be presented w evidence of extenuating circumstances, and be as to say whether these were sufficient, in their opin to make a death sentence inappropriate The system, they say, is found to work well on the wh in countries where it has been adopted Whet such a system would be acceptable here is a mat for discussion with the legal profession, but it noteworthy that the commission believe that, it is not acceptable, this country has reached a st at which little more can be done effectively to the liability to suffer the death penalty The is would then become whether capital punishment sho be retained or abolished And, indeed, we belie this to be the live issue It seems that the mission have worked very hard and conscientio to find ways of reducing judicial executions in system where they are already as limited as exis law allows Their recommendations would red the numbers sentenced to death and then repri (which would be an unquestionable gain), and wo also reduce slightly the number at present exec —particularly among those who are mentally a but not insane, in so far as these can be detected present psychological methods The public consc might then revolt against sparing the untreat psychopath and executing the sane man, pos capable of reform But surely it is time to be d altogether with a penalty which can never do m than rough justice to any criminal, which al always entails suffering to innocent people, and wh helps to keep murder and murderers perpetually in limelight

Annotations

EPIDEMIC VOMITING

"EPIDEMIC vomiting" ("epidemic nausea," "w vomiting disease") is an entity on its own, and seve striking epidemics have been recorded in the past years, notably in girls' schools[1–3] Webster[4] has recorded another epidemic of some 313 cases in a g school This began at the end of September, sk rose to an explosive peak on Oct 11, and faded gradually over the next few days The illness confined to the school and family contacts, and these groups the attack-rate was high It appeared be spread by close personal contact, and to have incubation-period of less than 5 days The not symptoms were abrupt onset of vomiting, gener with profound prostration (75% of cases), na (28%), headache (40%), abdominal pain (5 giddiness (36%), and diarrhœa, slight and transi with only one or two loose stools (30%) People of ages were attacked and the clinical features w constant throughout the whole age range The dura of symptoms varied from a few hours up to a day or recovery was rapid, and there were no sequelæ In outbreak there seemed to be no associated upper res tory infection There was nothing to suggest infe from the school water-supply or even from the s canteen, and, as in other outbreaks, the infection thought to be airborne Such virus studies as were d on blood and nasal washings yielded negative results

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1 Bradley, W H *Brit. med J* 1943 1, 309
2 Silverton M I *Med Offr* 1952, 88 215
3 Dummer F H M *Ibid* 1953 89 65
4 Webster R C *Ibid* 1953 90, 30.

Out of the welter of ill-defined acute virus infections which seem to exist in this and other countries, this mild winter epidemic infection seems to be qualifying for general recognition.

'URÆMIC LUNG—FLUID LUNG?"

In an article under this heading Alwall et al[1] answer their own question by saying that this is the first of a series on 'electrolyte-fluid retention Neither of the two names is particularly pleasing since the disturbance that they describe has often been observed in patients without uræmia, while a fluid lung' is literally impossible But the fact that exception can be taken to both these terms does not mean that a more suitable name is easily devised. Pathologists agree that the type of œdema found in the lungs is non specific and the syndrome could be defined as acute localised pulmonary œdema with X ray shadowing in association with acute fluid retention and left ventricular failure —a description that can hardly be shortened except by omitting one or other feature which differentiates this from other syndromes more or less closely related to it.

This type of acute localised pulmonary œdema was first reported in the 30s by Continental workers[2,3], who found it in association with renal failure and hypertension and ve it the name ' uræmic œdema. This name it has w retained with dwindling justification for twenty ars In 1941 the typical radiographic appearance was scribed of fan-shaped opacities radiating from the lum, but tending to spare the peripheral lung fields.[4] oniach,[5] who examined the lungs in four cases, found non infective albuminous and fibrinous pulmonary dema in various stages of organisation He pointed it[6] that the same type of œdema could occur apart om uræmia—for example, with cardiac failure due to yocardial infarction or mitral stenosis Pathologically e changes could not be distinguished from those of -called rheumatic pneumonia' He added that the peculiar butterfly shaped distribution of the transudate the lungs remains an enigma. Bass and Singer[7] ere perhaps the first to emphasise the importance of ft ventricular failure, noting the disappearance of the tered lung shadows as this responded to treatment they so cited Dock s explanation of the distribution of œdema ased on the relative immobility of the hilar parts of e lung by comparison with the periphery in which entilation might hinder the accumulation of fluid.

Alwall and his colleagues now bring forward clinical nd experimental evidence confirming the importance of uid retention in causing this type of pulmonary œdema hey studied fourteen patients with chronic renal failure nd two with anuria from acute tubular necrosis, all of hom were notably dyspnœic and had the characteristic adiographic appearances. Diarrhœa was induced by a aily dose of 200–400 ml. of 25% or 50% sodium sulphate o other fluid being given if the patient vomited, 100 ml f 25% sodium sulphate was given as an enema three or our times daily On this stern régime the patients eight fell by as much as 4 kg a day there was a ramatic recession of the pulmonary shadowing and yspnœa was relieved In experiments on rabbits the reters were ligated, a control radiograph was taken and n amount of "liquid corresponding to 15% of the ody weight was infused radiographic examination then howed extensive pulmonary shadowing which dis ppeared when the excess of body fluid was removed by ialysis In an addendum to their paper they mention he removal of a life menacing pulmonary œdema by five hours treatment with Alwall s type of artificial kidney[8]

Although retention of fluid may clearly precipitate acute localised pulmonary œdema many patients with massive œdema, as in type-II nephritis, have no dyspnœa and no pulmonary shadowing—suggesting that some additional factor promotes localisation of part of the excess fluid in the lungs The frequency of this type of pulmonary change not only in chronic nephritis, in which it was first described, but also in anuria and acute nephritis, suggests that this additional factor may be left ventricular failure secondary to hypertension The importance of cardiac failure has recently been emphasised both in anuria[9] and in acute nephritis[10] The recognition of acute localised pulmonary œdema is perhaps more important in these acute and reversible conditions than in chronic renal failure and the possibility of it strengthens the case for fluid restriction and complete bed rest in the management of anuria and acute nephritis

MENTAL NURSING IN DECLINE

Of the hospital beds in this country no less than 40% are in mental hospitals but this large group does not command anything like its proper proportion of our nursing resources. As is now widely recognised, the nursing service of mental hospitals though it includes many first-class men and women, is, in general insufficient and therefore poor Since trained staff are few, and recruits for training are getting fewer much of the burden of mental nursing is carried by people for whom no systematic course of training is at present laid down[11] This is a dangerous situation we could easily slip back to the cruelty and degradation of the old bedlams from which we are little more than a century removed.

A contributor to the *Male Nurses Journal*[12] makes some constructive suggestions He points out that many of the old chronic patients in mental hospitals do not need any mental nursing at all—only kindly care and general nursing of the type given in the geriatric wards of a general hospital or in rest homes for the aged. Such patients might well be transferred to such wards and homes, thus releasing beds for acutely ill mental patients likely to benefit by modern treatment Accommodation of the type suggested, however is still very scarce it would have to be greatly extended before this proposal could be put into practice Nevertheless, it would certainly promote economy in the use of qualified mental nurses and help to ensure that they were doing the work for which they were trained

Like us, this writer believes that student nurses in general training might well spend three months in mental hospitals This plan, we have suggested, might be tried first at Hill End, St Albans, where a teaching general hospital (St. Bartholomew's) and a mental hospital are already sharing the same buildings[13] He also proposes an interchange of administrators between general and mental hospitals, so that they may get a better grasp of each other s background and problems, and thus come to coöperate more easily In the manner of the *Prime Minister* in the days when he offered us blood and tears he calls for posters pointing out that nurses are needed in mental hospitals and that it is hard work demanding courage and patience. As a long term policy he advocates converting the mental hospitals into hospitals for the treatment of organic and functional nervous disorders (which would naturally include mental disorders) Such a hospital would carry neurological wards as well as wards for the neurotic and psychotic and would have an associated research unit The name of the hospital could then be changed to Somebody s Hospital for

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Alwall, N., Lunderquist A Olsson, O *Acta med. scand* 1953 146 157
Rubler C., Plauchu, M *Arch. méd chir Appar resp* 1931 9 189
Klima, R. Rosenzer H *Med. Klin.* 1936 32, 85
Hendich, R. A., Levy A. H., Cove, A M. *Amer J Roentgenol.* 1941 46, 802.
Doniach I *Ibid* 1947 58, 620
Doniach I *Lancet*, 1949, ii, 911
Bass, H. R., Singer E. *J Amer med Ass.* 1947 144 819

8 Alwall, N *Acta med scand.* 1947 128 317
9 Swann, R. C., Merrill, J P *Medicine Baltimore* 1953 32 215
10 Peters J P *Amer J Med.* 1953 14 448
11 *Lancet*, July 25 1953 p 177
12 September–October 1953 p 13.
13. *Lancet*, 1953 i, 641

Nervous Disorders", and thus, as he says, would soon be contracted to "Somebody's Hospital," and the term "mental nurse" to plain "nurse"—the most sensible name

Meanwhile recruitment to the mental nursing service could be fostered, he thinks, if the trained staff and the public were in closer touch The hospitals could hold open days, with full civic and press support, when visitors would be taken round the wards and laboratories on conducted tours Trained staff could give talks to women's institutes, senior schools, associations of teachers, and industrial and youth organisations Patients who are well enough could attend local meetings in which they are interested—of church groups, Women's Voluntary Service, farmers' unions, and clubs, as well as educational and Red Cross courses The leagues of Friends of Mental Hospitals should be helped to extend their activities to all parts of the country, where they are active they are already doing much to create good feeling between the hospitals and the public Such increased commerce between the hospital and the outside world would help to break down the isolation in which the mental hospital residents—patients and staff alike—at present live The hospitals are isolated in another sense each of them is a separate community, with its own customs and methods, and there is very little interchange of ideas—anyhow of nursing ideas—between one hospital and another It is a long-standing weakness of the service, which might be overcome more easily if there was some coordinating body—some association or group to which all mental hospitals belonged—which would publish information about the work of its various members

TINEA CAPITIS

THOSE dismayed by the advancing tide of warts may feel that the employment of a squad of reliable wart-charmers would be a legitimate charge on public funds The activities of the Ulster ringworm charmers [1] are less admirable Their good reputation, like that of some more orthodox practitioners, rests on the tendency of some diseases to get better without treatment This happens particularly often in human infections with ringworm fungi normally parasitic on animals

In dealing with a large epidemic of ringworm in Northern Ireland, Beare and Cheeseman [1] found it unnecessary to treat cases of tinea capitis due to *Microsporum canis* by the conventional method of X-ray epilation this they reserved for cases due to *M audouini* and *Trichophyton sulphureum* *M canis* infects kittens, which are the main reservoir of contagion Beare and Cheeseman's maps showing the distribution of their cases in Belfast indicate clearly that infections with *M canis* were sporadic, whereas those due to *M audouini* were concentrated in two main areas, suggesting case to case spread This is the usual experience, although according to Kligman [2] *M canis* can cause wider outbreaks when it mimics *M audouini* by producing non-inflammatory lesions with less tendency to rapid spontaneous healing

Thomas [3] has also reported that it is not essential either to treat *M canis* infection with X rays nor to keep infected children from school Whittle [4] has witnessed an epidemic of scalp infection with *M audouini* in which most cases responded to simple local measures It is true that he was dealing with a rather feeble variant of the parasite, but it is valuable to know that such variations in virulence occur Kligman's work, the most interesting on the pathogenesis of tinea capitis since the days of Sabouraud and Adamson, shows how far the course of infection may depart from what is usually expected

The main object in insisting on treatment is to protect not so much the patient as the community Beare and Cheeseman's report illustrates how careful clinical examination, good contact tracing, mycological investigation, and prompt treatment can curtail epidemics X-ray epilation is not the ideal routine treatment, for it requires faultlessly calibrated machines and skilled operators experienced in the technique, if disproportionate risks are not to be taken Dermatologists look forward to the development of antibiotics effective against fungi Those causing the various forms of ringworm live exclusively in keratin, and a substance may be found which, excreted by the horny layer, nails and hair, will offer the parasites their hemlock disguised as a favourite metabolite

GREAT EXPLORATIONS

Sir Henry Dale's friends have fortunately been able to persuade him to make, and to issue in one volume,[1] his own choice of his published writings He has written a charming and illuminating introduction, and has added retrospective commentaries to the individual papers These papers are landmarks in an eventful career some are also landmarks in the history of science In 1910 Barger and Dale introduced the word "sympathomimetic" to describe the action of various amines which parallel, in varying degree, the excitatory and inhibitory effects of sympathetic-nerve stimulation In 1914 Dale first described the pharmacology of acetylcholine, which his colleague Ewins had isolated from ergot, and drew attention to its muscarine like and nicotine like aspects In 1929 Dale and Dudley, searching for histamine in the spleens of ox and horse, detected enormous choline-like activity and announced the first chemical isolation of acetylcholine from animal tissue In 1933 Dale proposed the terms "adrenergic" and "cholinergic" There followed the well known papers, with Brown, Feldberg, Gaddum, and Vogt, on cholinergic transmission, the subject with which Dale's name is linked by every student of physiology in the world today

For the experimental pathologist another set of landmarks stands out In 1910 Dale and Laidlaw first described the pharmacology of histamine, noted the different distribution of its stimulating effect on plain muscle in a variety of species, and cautiously compared these actions with the phenomena of anaphylaxis In 1913 Dale found that plain muscle from a sensitised guineapig would contract if treated in vitro with a minute dose of antigen In 1922, Dale and Kellaway proved that such plain muscle would not contract to added antigen if free antibody were present in the bath And in 1927 Best, Dale, Dudley, and Thorpe isolated histamine chemically from liver and lung

Medical men will be glad to have these thirty papers bound together for convenient reference, but it is to the beginner in research that the book should make its most special appeal, for the introduction and comments and, not less, the selection and juxtaposition of the papers give unique insight into the scientist's work, into the growth of his ideas and of his skills Sir Henry tells some fascinating stories of lucky accidents with ergot and liver extracts and with sensitised guineapigs thought by others to be good enough for pharmacological experiments, but his assessment of the large part played by such accidents in his success will not be taken very seriously Many will suspect that they themselves have had similar opportunities and not known it The comments are models of modesty He blames himself for not having tested noradrenaline in 1910, when it was commercially available as 'Arterrenol' Of discovery in 1920 that adrenalectomy increases enormously the susceptibility to histamine shock he writes today ' My purely speculative suggestion of an unknown function of the suprarenal cortex might be made to assume a certain air of prediction if viewed in the light of what is now known but the fact that I made no attempt to follow that line of thought by further experiments, is sufficient evidence that I myself attached no serious importance to it at that time ' Exemplary caution in the use of drugs as physiological tools is shown in the paper with Laidlaw in 1912, in which it was proved that dilatation of the pupil by nicotine is not due as might have been thought, to direct action of nicotine on the pupil, but is due to stimulation of the adrenal medulla But perhaps the most important lesson here illustrated is that taught by Ramon y Cajal the need to ponder for years on particular subject-matter to achieve a degree of cerebral polarisation ' if important progress is to be made Thus, over years, the idea of chemical transmission took hold first for the autonomic, then for the somatic nervous system The conception of a rapid localised liberation and removal of acetylcholine has provoked, and been abundantly confirmed by, newer electrophysiological experiments which have accurately defined the conditions of synaptic and neuromuscular transmission

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[1] Beare J M., Cheeseman, L A. *Ulster med J* May 1953 22, suppl

[2] Kligman A M. *J invest Derm* 1952 18, 231

[3] Thomas B A. *Brit med J* 1953 1 536

[4] Whittle, C H. *Lancet* July 4 1953 p 10

[1] Adventures in Physiology with excursions into autopharmacology A selection from the scientific publications of Sir HENRY HALLETT DALE, O.M, G B E, F R S, M.D, F.R.C.P. With an Introduction and recent comments by the Author London Pergamon Press 1953 Pp 652 £6 6s

LABORATORY DIAGNOSIS OF SMALLPOX

THE cost of this country s freedom from smallpox —constant vigilance—is buried in the expense of the preventive services generally When the disease is detected at the ports and still more when it slips through the cordon energy is diverted to its control and the cost soars. An expensive administration comes into action The cost of vaccination, surveillance and hospital care can be readily measured but the toll on the national energy exacted by public apprehension cannot be estimated Confronted with a doubtful case of smallpox the medical administrator must choose between the risky policy of waiting and the expensive policy of action *The emergence of reliable laboratory tests has reduced materially the period of doubt* instead of depending on protracted clinical observation in a smallpox hospital, he can do tests which rapidly and convincingly aid the diagnosis often without moving the patient

The Ministry of Health has issued a brochure [1] on the laboratory diagnosis of smallpox for the information of medical officers of health medical officers of seaports and airports, and others who may be concerned in the diagnosis of the disease. The document includes notes on the tests available a reproduction of an article by MacCallum,[2] instructions for collecting and dispatching specimens, a list of laboratories available for performing the tests, and a list of the Ministry's clinical consultants in smallpox The limitations of the laboratory methods are noted, and emphasis is placed on the tests as aids to clinical diagnosis, not as substitutes for it.

The most useful tests are those in which the virus or its antigen is sought in the local lesions Direct microscopic examination of smears from early lesions rapidly confirms a clinical diagnosis but a negative result does not exclude the disease and the test is not reliable from the pustular stage onwards The complement fixation test is much more reliable and provides a result in twenty four hours. The suspected material (papule scraping vesicle fluid, or crusts) is used as antigen against a known rabbit-serum The third test is egg culture of the suspected material; the result is known in 48–72 hours. Occasionally egg-culture from the blood of febrile contacts in whom the disease is developing may give a diagnostic growth by the time the rash appears Tests for antibodies are less helpful because antibodies do not appear until the seventh day and recent vaccination interferes with the tests

With these aids the clinician is more favourably placed than he has ever been before In future every case in which a reasonable suspicion of smallpox arises will, no doubt be subjected to such tests Mistakes will still be made but they are likely to be less common and much less disturbing to the public

BACTERIAL L FORMS

THE obscurity surrounding the L forms of bacteria is due partly to technical difficulties and partly to the semantic problems which bedevil discussion of their origin fate and significance Pulvertaft [1] has made a commendable attempt to clear up some of the difficulties by proposing that The name L form should be used to describe the large plastic masses How far this restriction usage will find favour it is difficult to say From Klieneberger s first report in 1935 [2] onwards the definition has been very vague

Thus Klieneberger wrote Organisms L_1 and L_2 the structure and life cycle resemble closely the morphological development of pleuropneumonia Dienes [3] wrote of L type variants in cultures of various bacteria and of tiny secondary colonies similar in appearance and morphology to the L_1 variant of *Streptobacillus moniliformis* Dienes and Weinberger [4] stated: The peculiar forms which are the subject of this review are called L forms and their colonies and cultures are referred to as L type They continue:

In the description of the morphology of L type cultures the terms Small forms Swollen forms, and Large bodies are employed The latter two terms will be applied also to pleomorphic forms of bacteria Later in the same article they wrote the L forms grow from the large bodies as strands of refractile granules, and the large bodies either return to bacteria or grow into L forms

This appears to equate the L bodies with the small forms On the other hand Klieneberger Nobel in 1949 [5] said that the size and shape of the L bodies largely depended on the number and arrangement of the primary cell units, ' and referred to a large disc like body which because of its shape, size and structure must be regarded as an L body In a later paper photomicrographs of L bodies give the impression that these are small, pleomorphic masses.[6]

More recent accounts have done little to clear up the difficulties of interpretation The reports by Wittler [7,8] on the L form of *Hæmophilus pertussis* seem to refer to pleomorphic masses equal to or larger than the bacterial forms. Pulvertaft s report on the effect of antibiotics on growing cultures of *Bacterium coli* [9] contains a very good account of usage of the term L forms and appears to distinguish filamentous forms from L forms The usage in Stempen and Hutchinson s [10] account of large bodies in *Proteus vulgaris* is that adopted by Pulvertaft in his latest paper [1] but Dienes and Zamecnik [11] last year differentiated large bodies from L forms. Lately Howard Hughes [12] discussing L variants of *Bact. coli* has introduced yet another conception The essential feature of an L variant would be that growth continued while division was inhibited

Various workers claim to have found L forms in urine and Wittler [8] showed that *H pertussis* was in the L form when infecting mice. There is good evidence that L forms are more resistant to penicillin and other injurious

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1 Mem. Port 21
2 MacCallum F O *J R sanit. Inst* 195 72 112.

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1 Pulvertaft, R. J V. *J Path Bact* 1953 65 175
2 Klieneberger E. *Ibid* 1935 40 93
3. Dienes, L. *Proc Soc exp Biol*, N Y 1939, 42 636.
4 Dienes, L., Weinberger H J *Bact Rev* 1951 15 245
5 Klieneberger-Nobel E. *J gen Microbiol* 1949 3 434
6 Klieneberger-Nobel, E. *Ibid* 1951 5 525
7 Wittler R G *Ibid* p 1024
8 Wittler R. G *Ibid*, 1952 6 311
9 Pulvertaft, R. J V *J Path Bact* 1952 64, 75
10 Stempen, H , Hutchinson W G *J Bact* 1951 61 337
11 Dienes, L , Zamecnik, P C. *Ibid* 1952 64 770
12. Howard Hughes, W *J gen. Microbiol*. 1953 8 307

substances than the normal vegetative forms[7] An examination of the forms in which penicillin resistant organisms appear in vivo would be of interest, as also would be an examination of cultures that are being rendered penicillin-resistant in vitro Meanwhile we still need agreed definitions of the terms L forms, L bodies, L type cultures, small forms, and swollen forms

CHEST WOUNDS IN WAR

CHEST wounds have always been one of the most lethal injuries in warfare Sauerbruch, examining in 1914 the cause of death in 300 soldiers, found that 37% of them had died of gunshot wounds in the chest It is estimated that during the hostilities in Korea one-third to a half of all the men killed died as a result of wounds in the thorax, and that in the exposed forward area thoracic injuries are twice as common as abdominal Nevertheless, for the injured man who survives the original shock and damage, the chances of recovery have dramatically improved It is estimated that in the first world war 27% of soldiers with chest wounds died, but in the second world war only 8% The circumstances of the different fields of war have to be taken into account, but the improvement is undoubtedly due largely to improved methods of treatment

King and Harris[16] have now described their experiences with 405 major thoracic casualties in Korea As soon as an injured man is brought under medical care a decision has to be made as to whether he requires emergency treatment or can be treated more satisfactorily after evacuation to the base Emergency treatment is needed for such complications as continued bleeding, abdominothoracic injuries, and pressure effects which require relief For these, immediate operation is imperative, and in this Korean series, which concerns mainly the U S Navy and Marines, 52 thoracotomies and 43 laparotomies were done in the forward area The majority of the wounded were, however, the victims of hæmothorax, which was most satisfactorily treated on return to base, and the average time between the injury and the definitive treatment in this series was 7 days Hæmothorax is the principal factor in chest wounds Treatment should consist in early and complete aspiration, with the knowledge that this can be undertaken without any fear of starting further hæmorrhage King and Harris, who emphasise the importance of this early and complete aspiration, found that on an average they aspirated each of their patients three times, withdrawing almost a litre of fluid blood each time, but one patient was needled sixty times before the fluid was completely removed and the pleural space obliterated by re expansion of the lung An earlier belief, that aspiration could be accompanied by air replacement, should be discarded, because this measure does not encourage the lung to re-expand, and as a result a dead space is formed which may be the site of secondary clotting and infection If all aspirations are kept closed, and the fluid is withdrawn without any air being admitted, the lung will inevitably re expand and reach its proper position against the chest wall

King and Harris feel that the operation of decortication or pleurectomy, which found favour towards the end of the late war, is unnecessary if efficient closed aspiration is carried out, and they did this operation only 4 times Their use of $^1/_2$% acetic acid and 15% glycerin in normal saline as an irrigating agent was felt to be of value in facilitating aspiration and preventing infection, which is likely to arise in a long-standing hæmothorax There were only 25 examples of infection—owing, partly, to the continuous use of antibiotics 80% of their patients recovered completely and were fit for duty in 90 days The success of these methods may be judged by the fact that the mortality was only 1% Such results are obtained only with great patience and care

"FABER"

ANYONE who has tried to define a term, describe a method, or summarise a hypothesis has reason to understand the difficulty of compiling a dictionary containing thousands upon thousands of definitions, descriptions and summaries But, though they can never be perfect dictionaries are essential tools of learning, and in medicine as elsewhere it is very necessary that we should possess such tools, well constructed and kept sharp by frequent revision The *Faber Medical Dictionary*,[1] which made its first appearance last week, should be useful not only to doctors, dentists, and nurses but also to the many other people working in the National Health Service and elsewhere who are continually confronted with medical terms The profession throughout the English-speaking world has been well served by American dictionaries of high merit, but to those of us who read and write in this country it is no small satisfaction to possess at last a work of comparable scope which is British in its spelling and usage

Sir Cecil Wakeley, F R C S, the editor, and his associates, give us a large but easily handled volume of the kind that lures the reader away from his proper business Aiming at comprehensiveness, Sir Cecil has provided much that is unfamiliar and entertaining, and of course he is justified in so far as one of the functions of a dictionary is to explain words that ordinary people do not know by sight On the other hand he has put in a great many terms which, if they have ever really been alive few of us would wish to see brought back from the dead and if these were excluded from the next edition there would be room for more of the up to date information which is a feature of the work If, as at present, an attempt is made to include the better known proprietary names of drugs, the selection might well be larger, and though there is much to be said for making each item sufficient unto itself, there should always be cross references between proprietary and official names (For example Pentothal should be linked to Thiopentone) Further it would surely be convenient if this British dictionary made use invariably of the names approved by the British Pharmacopœia Commission (There are entries under Desoxycorticosterone, and Deoxycorticosterone and DOCA, but not under Deoxycortone, the *B.P* term An impression given by casual perusal is that the advancing science of endocrinology does not in fact get as much attention as do monsters in their infinite variety thus Cortisone is rather curtly dismissed as "one of the hormones of the adrenal gland used in the treatment of rheumatoid arthritis," and there is no mention of compound F On the long and entertaining controversy over "trophic" and "-tropic" hormones, "Faber" speaks with a certain ambiguity we find both Adrenocorticotrophic and Adrenocorticotropic (though the derivation here does not mention *trephein*), but neither of the adjectives Thyrotrophic and Thyrotropic gets an entry, though the latter is used in describing thyroxine We must take note, however, that another long contest has ended by Radiograph finally knocking out Radiogram Though the better man, the latter made the mistake of fulfilling engagements elsewhere

Taking the offensive, perhaps, against potential critics Sir Cecil and his colleagues describe Pessimism as "a neurotic disposition always to see and to expect the worst" This downright definition, though it omits philosophical conceptions, fulfils at least the editor's aim to be concise and readily intelligible It illustrates the robust good sense which initiated and infuses his book and which will win it many friends

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DR R H CROWLEY, a former senior medical officer of the Board of Education, died on Sept 25 at the age of

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[16] King J D Harris J H *Surg Gynec Obstet* 1953, 97, 199

[1] Faber Medical Dictionary Edited by Sir CECIL WAKELEY, F R.C S London Faber & Faber Pp 471 45s

International Conferences

MICROBIOLOGY

FROM A VIROLOGIST

At the 6th International Congress of Microbiology held in Rome during the week of Sept 6 2000 delegates gathered from all over the world to meet their colleagues from foreign countries, discuss their scientific problems and listen to some 1200 scientific communications Faced with such formidable numbers of delegates and communications, many organisations would have wilted The Italian organising committee, under its secretary general E Biocca might have been forgiven had they decided to hold the meetings at the Colosseum and throw the speakers into the arena instead they made a magnificent job of steering a large congress through a most complicated scientific and social programme

When the delegates registered for the proceedings they received among handsome gifts, three volumes of summaries of the communications weighing 6½ lb, and a guide-book and leaflets to help them to find their way through this maze of scientific knowledge At past microbiological congresses it has been possible for delegates, if they wished, to keep an eye on the main events taking place in perhaps five or six sections running simultaneously But the 6th congress found it necessary to divide itself up into 22 sections, and in addition a number of symposia were run at the same time As a result, even the most enthusiastic delegate had great difficulty in finding out what was happening even in his own small specialty Truly Dame Microbiology has developed a middle-aged spread—probably the result of ingesting too many scientific papers. There is a great need to remove some of her unsightly bulges before the next congress, but ways of doing so are by no means easy to prescribe Perhaps one method would be to have all communications published in the proceedings but to limit the number of communications to be read at the congress. Each country might be allotted a quota of communications to be read, and national committees would then select the required number from the communications submitted Such a plan has many disadvantages yet some such arrangement is urgently required if future congresses are not to develop into Microbiological Towers of Babel. A scheme of this type might also help to remove anomalies such as the reading of seven successive papers by one delegate.

Many must have been disappointed that only a small number of microbiologists from the U.S.A were able to attend. On the other hand it was good to see delegates from Russia, Poland, Czechoslovakia, and Hungary once more.

Work on Viruses

Faced with such a large variety of subjects there was nothing to be done except to show the most resolute single-mindedness by choosing one section and attending it regularly, the discriminating chose the section on animal viruses

T Wesslen (Stockholm) described a method of growing vaccinia virus in tissue culture of bovine embryonic tissue Embryos are easily obtained from the slaughter house and Wesslen's technique seems to offer a simple and cheap method of producing bacteriologically sterile vaccine It will be interesting to see the results of human vaccination tests with the tissue-culture virus.

A. W Downie and D R W Haddock (Liverpool) reported a variant of cowpox virus which differed from the parent virus in cultural characteristics and showed reduced animal pathogenicity It was interesting to find that from apparently pure cultures of the parent virus variants occurred with an average frequency of about 1 in 130 This surprisingly high figure might have made bacterial geneticists pause and wonder

A Macdonald and K. McCarthy (Liverpool) discussed natural heat labile inhibitors of a number of viruses present in normal animal and human serum and suggested that they might play a part in protecting against infection with small doses of virus

J B Brooksby (Pirbright, England) showed how the tissue-culture technique of Fulton and Armitage could be applied to the titration of foot-and mouth-disease virus—a method which should prove of great value in the study of this most difficult disease.

R Lundström (Stockholm) estimated the risk of immaturity congenital abnormalities and stillbirth as three times greater in the children of mothers who had contracted rubella during the first to fourth months of pregnancy than in those of controls Contacts of cases of rubella who were previously immune also showed an increased proportion of congenital abnormalities in their children C H Andrewes F.R.S found this difficult to reconcile with the protective action of gamma globulin against rubella and it seemed possible that the small numbers of cases might have created this impression

M M Sigel, A. J Girard and E G Allen (Philadelphia) studied the mode of multiplication of meningopneumonitis virus and found that the latent period of virus growth could be greatly prolonged by treating the tissues with aureomycin

C H Andrewes D Chapronière, A Gompels, H G Pereira and A T Roden (Salisbury England) announced to a most attentive audience their finding that the common-cold virus had been cultivated in tissue cultures of human embryo lung [1]

H B Donald Alick Isaacs and Forrest Fulton (London) confounded the mathematicians and philosophers with their conclusion that at least ten influenza virus particles were required to constitute one infective dose and Fulton and Isaacs showed that when incomplete virus was grown on the chick chorion it showed unexpected signs of life H P Chu (Cambridge) reported that the viruses of the influenza group agglutinated spermatozoa

H L Wolff (Leyden) observed that adults who had previously had mumps in childhood react on contact with the virus by producing a rapid increase in complement-fixing antibody He used this in order to make an early serological diagnosis of mumps By examining the patient's serum and that of his parents, nurses &c Wolff is often able to reach an accurate diagnosis of mumps on the first day of illness.

I Archetti (Rome) compared neutralisation and agglutination inhibition tests in the study of influenza vaccines and found the former a more sensitive method.

POLIOMYELITIS

The recent technical advances in the study of poliomyelitis were reflected in many interesting communications and discussions on this subject. J D Verlinde (Leyden) described the distribution of the three types of poliomyelitis virus in Holland; and he stimulated discussion of this subject by speakers from France Sweden South Africa, and the U.S.A Although the types were differently distributed in these countries there seemed to be general agreement that type 1 virus was the commonest and that type 2 virus tended to be associated with sporadic cases.

A B Sabin J Winsser, and W A Hennessen (Cincinnati) had some extremely interesting findings on what they called the pathogenic spectrum of poliomyelitis viruses in different tissues Poliomyelitis virus strains after continual cultivation in one tissue showed increased pathogenicity for that tissue but greatly reduced pathogenicity for tissues to which they had earlier been adapted Clearly this is a field of great importance for those seeking stable avirulent variants of poliomyelitis viruses for use in vaccines, and the phenomenon will repay careful investigation with all the virological, genetic, and serological techniques available

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[1] See Lancet Sept. 12 1953 p 546

G BARSKI, V MONACI, and M ENDO (Paris) have recently reported that that most dispensable of human organs, the tonsil, provides a convenient source of fibroblasts for cultivating poliomyelitis virus in vitro, and these cells have been most useful for a study of the detailed histopathology of the virus lesion

TH FRANCIS, jun, and L W CHU (Ann Arbor, Michigan) found that poliomyelitis virus was adsorbed to tissue constituents of the grey matter of the brain of monkey and man Other tissues of these animals or the same tissues from other animals did not absorb the virus This "receptor like" substance appears to be protein in nature and may prove a valuable object in the study of poliomyelitis-virus growth

A J RHODES (Toronto) described the use of synthetic nutrient media in tissue cultures infected with poliomyelitis virus Those who discussed his paper seemed curiously unimpressed with the advantages of having a medium of known chemical composition, but Rhodes produced sound theoretical reasons for his choice

J L MELNICK, J T. RIORDAN, E C CURNEN, and A D MACRAE (New Haven, Connecticut) found a number of unidentified pathogenic agents during their attempts to isolate poliomyelitis virus in tissue culture, some of these may be new viruses, but there is always the possibility that an unidentified agent may be a weakly pathogenic variety of a known agent or a mixture of two known viruses

A SVEDMYR and L KJELLEN (Stockholm) discussed their experiences with the complement fixation reaction in poliomyelitis using antigens prepared from tissue culture virus by improved techniques

D HORSTMANN and R W, MCCOLLUM (New Haven, Connecticut) demonstrated the occurrence of viræmia during poliomyelitis and pointed out that the beneficial action of gamma globulin in poliomyelitis is not necessarily due to its stopping the viræmia

S GARD (Stockholm) found that during the late stage of an epidemic of poliomyelitis quite a high proportion of infants and young children, but not adults, excreted virus He assumed that the positive individuals represent a selection of persons not previously exposed to virus and suggested that the percentage of positives among the non immunes rather than of the whole population should be taken as significant of the rate of dissemination of virus in the community This, incidentally, may be one of the last epidemics in which isolation of poliomyelitis virus was made by inoculating monkeys

OTHER VIRUSES

J S F NIVEN, A W GLEDHILL, and G W A DICK (London) showed the dual character of the ætiology of mouse hepatitis *Eperythrozoön coccoides*, an organism with an unexpected ability to penetrate bacterial filters, was found to enhance greatly the pathogenic action of the mouse hepatitis virus and of a number of biologically related agents

R M TAYLOR (Cairo) described the isolation of a number of viruses from human blood and mosquitoes in Egypt He identified Coxsackie and West Nile encephalitis viruses and possible new agents

There were some rather sensational discoveries reported under the heading "diseases of possible virus ætiology," but it seems likely that the ætiology of many of these conditions will remain in doubt for some time

Symposia

In parallel with the congress, a number of symposia were organised by the Instituto Superiore di Sanita In perhaps the most stimulating paper R DULBECCO and M VOGT (Pasadena, California) described the techniques for studying the growth of animal viruses Previously workers with bacteriophages have enjoyed the advantages of being able to count the concentration of infective bacteriophage in a preparation by spreading it on a single suitably inoculated petri dish, and to measure by appropriate methods the yield of bacteriophage from a single cell Now Dulbecco has adapted these techniques to the study of animal viruses grown in tissue culture Animal viruses such as those of equine encephalomyelitis and poliomyelitis were found to produce plaques analogous to bacteriophage plaques when spread on the surface of a thin layer of tissue-culture cells grown on glass From such plaques it is possible to isolate pure "colonies" of virus and to envisage the carrying out of accurate genetic studies Dulbecco also carried out kinetic studies of the growth of virus in suspensions of separate cells and in single cells, and he found that the release of virus from these cells was gradual over a long period of time, unlike the sudden release of bacteriophage from bacteria on lysis. Both from the point of view of what was already accompl and from its future possibilities this was one of the most important contributions to the congress

R W SCHLESINGER (New York) gave a most stim account of the multiplication of influenza virus He was anxious to find some rational explanation for the enzyme action of influenza virus and saw in it some f nda activity connected with multiplication rather than accidental property of little practical value to the virus He presented interesting results to show the variation in concentration of the enzyme substrate during the course of infection, and concluded, as Dulbecco had de that the cells produced virus over quite a long period of time

P VON MAGNUS (Copenhagen) described his work with incomplete influenza virus, made in an attempt answer the puzzling question whether incomplete virus is an immature developmental form or mature but defective virus His exhaustive experiments cover almost every aspect of the phenomenon, and he presented reasoned accounts of the factors governing the appearance of incomplete virus He emphasised the heterogeneity among incomplete virus particles, and GARD, as result of his analyses of the lipid content of the virus forms, supported this strongly

Apart from the communications there were numerous formal and informal scientific meetings associated with the congress Thus the International Committee on Bacteriological Nomenclature decided that henceforth *Bacterium coli* should become *Escherichia coli* The subcommittee on virus nomenclature were less fortunate they agreed that Professor Gard should take the minutes and this represented the major area of their agreement Nevertheless the congress produced a great deal informal agreements, friendships made and renewed and collaborations established Italy was in many ways an ideal country for the congress, and the friendliness and sunny temperament of the Italian and his climate soon communicated themselves to the delegates

Perhaps the Italian motorist's method of indicating the direction he wished to go by driving straight at may have stimulated morbid reflections on the half of the Italian pedestrian, the leisurely progress of Italian waiters may have set in motion a few doubts as to the true meaning of the word *subito* Perhaps, too, scientists may have felt a little sad when they heard about difficulties which a young Italian may have to overcome if he wishes to pursue a research career, scientists this country are not accustomed today to hearing that young university workers may have to buy their own animals and apparatus if they wish to do research however they may have reacted to this or that a of Italian life, there were few delegates who left Rome without a deep impression of the beauty and majesty of a great city and a great civilisation

PHYSIOLOGY

FROM A CORRESPONDENT

MOST people associate Montreal with McGill and McGill with Osler But Penfield, Collip Meakins, Babkin and Browne have also made Montreal a world medical centre, and Masson and Selye have attracted budding histologists and experimental endocrinologists from all over the world to the young Université de Montréal which has become the French Canadian Sorbonne

The 19th International Physiological Congress, held in Montreal between Aug 31 and Sept 4, went off with élan. The atmosphere of the city is unique Although 65% of its population is of French Canadian descent its strategic position as the gateway to Canada filters out many Europeans who come to settle in the country In winter and in summer it is also a playground and business centre for Americans from New England and the East Coastal States Its flavour is a mixture of French Canadian glamour shrewdness and finesse of English Canada's adventurous foresight; and of American hustle and know how These attributes and the peculiar saltiness common to all great ports, have made it the cosmopolitan centre of North America—and a gay one at that.

Some 3000 members and associate members from 48 countries, including a large contingent from the United Kingdom, registered for the congress, which was notable for the tremendous amount of work presented and for the overwhelming hospitality of the Canadians.

Dr CHARLES BEST co-discoverer of insulin, in a presidential address opened the congress and also gave a display of verbal virtuosity in welcoming the members in six languages, including Gælic and Mohawk

During the week seven symposia were given in the Salle des Promotions of the Université de Montréal while over 700 individual papers and 60 demonstrations were given at McGill. Buses shuttled between the granite grey ivy walled, tree-shaded McGill campus and the barren yellowness of Montreal's modern university McGill has the classic veneer of any Scots university and flows down the commanding slope of Mount Royal into the centre of the city The Université de Montréal is built high on Mount Royal on the north western slope of the mountain overlooking the suburbs Its main building, a phallic tower rears a corona high above the factory modern classrooms and laboratory buildings which cluster around it

When one got tired of symposia and papers or needed relief from the heat there were lounges for talking or writing an open-air buffet under the trees for food or beer in the garden of the Arctic Institute of North America. The entertainment was magnificently organised All of 3000 guests were invited to cocktail or dinner parties given in the private homes of the hospitable medical community of the city Gay free-and-easy receptions were given to the congress by the Province of Quebec and by the City of Montreal, who gave two lavish evening parties in the chalet on top of Mount Royal. There were boat trips up and down the St Lawrence, fun fairs, a water ballet, and outings in the Laurentian Mountains. The wives went to fashion shows and on tours of Canadian industries including a brewery and were taken sight-seeing over Montreal by Trans Canada Airways.

At special convocations, honorary degrees were conferred on Prof W R. Hess, Sir Henry Dale O M., and Prof E Lundsgaard—all past presidents—by McGill University The Université de Montréal conferred degrees on Prof E D Adrian, O M and Prof L. Binet. Dr W W Francis director of McGill's Sir William Osler Library put on display the treasures of Osler's famous and unique historical collection, and the exhibit of early physiological books was particularly interesting

Officials of the International Council of Scientific Unions affiliated with UNESCO seized the opportunity to convene a constituent general assembly for organising an International Union of Physiological Sciences; and they also arranged a Symposium on the Future and Limitations of Physiological Research under the chairmanship of Professor Adrian

The amount of work presented at this congress was tremendous and much of it was clinical. The abstracts of communications were published in a 976 page book weighing nearly two pounds and containing over 1000 communications. Besides the official meetings demonstrations and films private group meetings were held for specialists in various subjects

Ten Russian physiologists headed by K M Bykov, attended the meeting Everyone was pleased to see that they mingled more freely with the other delegates than they did at the Copenhagen congress in 1950 They were neurophysiologists and in the main presented papers dealing with extensions of Pavlov's work These were given in Russian but they had brought with them translations of their communications in English and in French which were available to members of the congress Perusal of these papers and the abstracts shows that a tremendous amount of extremely interesting work on conditioned reflexes is being done in Russia Unfortunately, experiments and data are obscured by unnecessary polemics related to the deification of I P Pavlov, the conceptions of dialectic materialism, and the wickedness of Sherrington Fulton Magnus and Liddell It is a pity that in 1950 and 1953 we had only a small peek at a segment of Russian physiology No doubt they consider Pavlovian neurophysiology their most important contribution, but it is getting rather tiresome to those of us interested in other aspects of health and disease It would be nice if in 1956 we were allowed a peek at other aspects of Russian physiology such as studies on shock hæmorrhage blood coagulation, geriatrics and the physiology of cold—fields of endeavour in which Russian physiology presumably excels.

The symposia on Insulin, Hæmodynamics in Small Vessels Cardiac and Pulmonary Reflexes, Postural Mechanisms Physiology of Learning Formation of Thyroid Hormone and the Physiology of the Cold dealt in the main with reviews of published observations. Many of the individual communications were grouped together round specific subjects In some fields there have been tremendous advances or clarification in the past three years. Particularly impressive were the clarification of problems of blood coagulation and studies of the hyperglycæmic hormone from the pancreas—glucagon.

Elements in Wall of Blood vessels

A. C BURTON (Ontario) said that histological study shows four clearly defined types of tissue in the wall of blood vessels—namely the endothelial lining the various elastic tissue layers, the smooth muscle and the fibrous connective tissue which forms an outer tunic and penetrates between the last two tissues These elements are found in different proportions in the different types of blood vessels, and in the true capillaries only the first seems to be present Theoretical analysis with the aid of the classical law of LaPlace and indirect experimental evidence using the flow pressure relations in vascular beds, has given us a new appreciation of the rôle of each of these elements and their coöperation in the control of blood flow Semiquantitative estimates of the magnitude of the tensions developed in these tissues under the blood pressure and under vasomotor tone are now possible

Physiology and Pathology of Cerebral Cortex

K. M. BYKOV (Leningrad) stated that the three principles of I. P Pavlov's theory are determinism unity of analysis and synthesis, and unity of function and structure The physiologist and psychologist who follows Pavlov's teaching wages a relentless ideological struggle against representatives of metaphysical conceptions in physiology and psychology who, to date, are preaching dualism in the characteristics of processes taking place in the brain, contrasting the nervous process with the psychological, tearing it away from structure, denying to the nervous factor its main and determining rôle in all vegetative somatic processes, and attempting to restore an antiscientific subjective method of investigation Freud's idealistic conception, which has nothing in common with a scientific analysis of a normal or pathological disturbance of the activity of the functions of the central nervous system, is alien to the real physiology of the brain

Biochemical Observations on Inflammation in Rats

V W ADAMKIEWICZ (Montreal) said that a method was recently devised for studying inflammation in small laboratory animals This method—the "granuloma pouch" technique —is simple, and permits initiation of inflammation in an exactly reproducible and quantitative manner and production of large amounts of exudate which are well delimited by a considerable layer of granuloma tissue The exudate can be accurately measured and the granuloma weighed This technique does not cause much systemic stress since it is well tolerated even by hypophysectomised rats The exudate shows a high degree of constancy in its main chemical constituents within any experimental group hitherto investigated Using this technique, he studied the changes in various chemical components (proteins, sugars, fat, Na, K, Cl, P) in the exudate and granuloma when the course of inflammation was modified by hypophysectomy, adrenalectomy, treatment with prophlogistic hormones (corticotrophin, hydrocortisone, cortisone), and treatment with antiphlogistic hormones (deoxycortone acetate, somatotrophic hormone) Modifications in sugar and fat content were detected in the various exudates collected on the 14th day of inflammation Studies were also made on the permeability of the granuloma wall to ions (Na, K, Cl, P) and water during different stages of inflammation It was found that the granuloma wall is readily permeable to the ions. Finally, an attempt was made to show the triphasic nature of the response of the body to local injury The biochemical criteria used for this are the changes in concentration of Cl, P, Na, K, and the changes in water-clearances of connective tissue undergoing inflammation The triphasic nature of this "local adaptation syndrome" resembles that of the general adaptation syndrome

Incoagulable Afibrinogenæmic Blood

B ALEXANDER, R GOLDSTEIN, ANNE G LEBOLLOC'H, L K DIAMOND, and W BORGES (Boston, Mass) reported that studies on incoagulable blood from three subjects with congenital afibrinogenæmia have yielded information concerning basic aspects of the coagulation sequence independent of the fibrinogen fibrin system Immunochemical tests revealed at most only traces, and certainly less than 1% of normal, of fibrinogen or fibrinogen like material in the plasma After the blood is shed and exposed to glass, the earliest detectable changes, beginning within a few minutes, are morphologic alteration in the platelets and their progressive agglutination and lysis Almost in parallel, plasma antihæmophilic activity, originally normal, declines and practically disappears Also within minutes, Spca evolves from its precursor in normal manner Prothrombin disappears at normal velocity, or slightly faster than normal Ac globulin also disappears at normal rate The Ac globulin of afibrinogenæmic oxalated plasma is convertible to the active serum form by addition of thrombin Thrombin addition to the plasma also induces platelet agglutination, but this does not occur when thrombin is mixed with platelets alone Antithrombic activity of afibrinogenæmic plasma is normal The co factor of heparin antithrombin effect was demonstrable Quantitative data relating the fibrinogen concentration with the prothrombin time were obtained It may be concluded with reasonable certainty that conversion of fibrinogen to fibrin plays no rôle in the changes described above

Contractility of Human Uterus

H ALVAREZ and R CALDEYRO BARCIA (Montevideo) described studies of the pressure exerted by the uterine muscle on its contents, by recording the pressure of the amniotic fluid The coördination of the contraction is analysed by recording the intramuscular pressure in several parts of the by means of 4 microballoons inserted in the mass of the muscle and connected with a capacity manome During pregnancy localised contractions are produced th cause small and rhythmical oscillations in the amn pressure Sporadically a general contraction of the wh uterus appears In the days preceding labour the frequen of the generalised contractions increases progressively, w the number of the localised contractions decreases In norm labour there are generalised contractions which start fr the uterine end of one of the fallopian tubes, and spr very rapidly inwards and downwards (descending propa tion), all parts of the uterus contract with good synchro sation. The upper parts of the uterus contract stronger longer than the lower parts There are 3–5 contractions 10 minutes In the third stage of labour the record of t placental blood-pressure shows that the contractions ha the same characteristics as in the first and second stag though they are absolutely painless In the hours th follow labour, there is a progressive decrease in the of the contractions, and also in the propagation speed the contraction wave In abnormal labours the are observed (1) weak contractions, (2) bad coördinati with (*a*) lack of fundal dominance, (*b*) ascendent propagati of the contractions, (c) lack of synchronisation between t different parts, (*d*) localised contractions, and (3) hyperto produced by (*a*) over distension of the uterus, (*b*) asynchr nism, (c) high frequency of contractions (*d*) premat separation of the placenta

Physiological Responses to Aldrin

W. L BALL, K KAY, M CREVIER, and J W S (Ottawa) said that the possible ill effects on human bei of the recent tremendous increase in the use of chlorinat hydrocarbon insecticides is causing concern Aldrin w selected for investigation because it is the most toxic of common insecticides of this type In the preliminary st of the work it was demonstrated that it has growth stimula and œstrus inhibiting factors and causes organ enlargem and pathological changes A lowering of the basal meta lism and an increase in the serum esterase activity w observed All these effects occurred at dietary levels wh could result from the persistence of aldrin on foodst The rise in serum esterase caused by aldrin suggested it m antagonise the effect of the cholinesterase inhibitors. I pre-treatment of rats with aldrin produces fivefold protect against the organic phosphate insecticide, parathion

Sodium Excretion with Cardiac Disease

A C BARGER, R S ROSS, H L PRICE, G M. W and L BROOKS (Boston, Mass) investigated the ability excrete an infused load of isotonic sodium chloride in d with various experimentally produced valvular lesions of t heart In these animals the excretion of sodium chlo and water during the 8 hours immediately following a stand infusion is reduced to as low as 1% of preoperative con values Delayed excretion of sodium loads ac changes of cardiac function which produce little or no elevat of resting venous pressure, and no significant change in t ratio of infused sodium load to total exchangeable bo sodium was found

Carbohydrate Metabolism in Spinal-cord Injury

J M BERNSOHN, BROWN, and J R FINKLE (Hines Chicago, Illinois), studying the regulatory defects occurr in spinal cord injury, determined glucose tolerance curve 86 patients with spinal cord lesions at various levels, and a minimum of 15 months' duration. The results indic that while no differences in the fasting level were appar patients with spinal cord lesions in the cervical reg exhibited sustained high curves Statistical analysis of t results indicated that after the 30 minute period the va obtained in the cervical cases were all significantly hig than the other comparable values While the mechanism this dysregulation in carbohydrate metabolism is not c clusively demonstrated by the data, the results support concept that descending fibres from higher centres interrupted, and that this interruption may cause a function in the homœostatic mechanism involving the co of blood glucose levels

Goitre Prophylaxis with Iodised Salt

B E BRUSH (Detroit, Michigan) said that in 1923 a su of the school children in four Michigan counties, mad e State health department and the State medical society vealed that of 65,637 students 38·0% had goitre At the me of the goitre survey the amount of iodine in the soil d drinking water at various points throughout these unties was studied A close and constant relationship as noted in each instance in that the prevalence of goitre as in inverse proportion to the available iodine Following is, an extensive programme was begun to advertise the portance of iodised salt, which was placed on the market 1924 Subsequent surveys showed a remarkable decrease the prevalence of goitre in these same areas. In 1928 the er all prevalence was 9 0% and in 1951 only 1 4%. A record as made in these subsequent surveys of the number using dised salt, those not using it and those who used it part the time As was to be expected, there was a marked crease in goitre among those who had used iodised salt gularly and no decrease in those not using it

Metabolic Effects of Pituitary Growth hormone

A. Carballeira, H Elrick K R Mackenzie, and S L. Browne (Montreal) said that purified preparations pituitary growth hormone have been ineffective in man contrast to the striking metabolic effects produced in boratory animals. As these preparations have been adminis red either subcutaneously or intramuscularly with the ssibility of inactivation by tissue enzymes, the intravenous ute was chosen in these experiments. Under the influence growth hormone the rate of disappearance of injected mino-acids from the blood was accelerated. Urinary amino itrogen excretion was reduced in the growth hormone periments. The blood non protein nitrogen levels did not crease suggesting an incorporation of the amino acids into e tissues. A slight and transient rise in blood sugar levels as observed within the first 2 hours after the growth hormone as administered. The ketohæmia of fasting was also creased when growth hormone was used Serum phos-horus, alkaline phosphatase and urinary phosphorus owed no consistent change Eosinopenia was observed ith a dose of 3 mg per kg body weight but no significant anges occurred with the lower doses when compared with e control experiment Apart from nausea and vomiting, hich occurred in two subjects receiving the 3 mg per kg se, there were no untoward effects from the administration this preparation of growth hormone

Glucagon

C de Duve and C. A. Vuylsteke (Louvain, Belgium) id that glucagon (hyperglycæmic glycogenolytic factor of e pancreas) has been isolated with approximately tenfold rification from alkali inactivated insulin but has never en successfully separated from the native hormone In der to follow accurately the results of chemical fractiona ons, the assay on isolated rabbit-liver slices developed by therland and de Duve has been improved mainly by the clusion of a reference standard in the test and by the use logarithmically spaced doses, rendering the results amenable statistical analysis. By means of sodium-chloride frac-onation at pH 1·4 followed by fractional crystallisation, it s been possible to isolate preparations which have about n times the specific activity of the purest samples obtained Sutherland and co workers. Unfortunately the yields e small.

Toxicity of Serum and Urine

R Fischer (Regina, Saskatchewan) has tested the serum d urine of acute schizophrenics on larvæ of *Xenopus lævis* ed at 20°C; 10–20 ml per litre of serum or 25–60 ml per re of urine added to the water milieu of 14-day-old larvæ used a significantly higher mortality than the serum and ine of healthy controls in the same dilutions. Spontaneous mission or successful treatments gradually diminish the xicity to normal values Whether the toxicity of acute hizophrenic serum may be regarded as a consequence of e schizophrenic stress situation or might be in some way volved in the ætiology of schizophrenic psychopathology is ll uncertain.

Physiological Secretion of Glucagon

I P Foa Harriet R. Weinstein E. B Magid M. D ardman and J A. Smith (Chicago) investigated the hypo-esis that glucagon is a second hormone normally secreted the pancreas, by cross circulation of the pancreato-duodenal in of a donor dog with a femoral vein of a recipient dog jection of insulin in the donor dog was followed by hyperglycæmia in the recipient dog suggesting that the donor dog secreted glucagon in response to insulin hypoglycæmia The injection of glucagon into the donor dog was followed by hypoglycæmia in the other dog suggesting that the pancreas of the donor dog secreted insulin in response to glucagon hyperglycæmia These workers believe that secretion of glucagon is regulated by the blood-sugar level Their data indicate that pituitary growth hormone causes hyperglycæmia by stimulating the secretion of glucagon. This may explain, in part the diabetogenic action of growth hormone

Furadantin in Urinary Proteus Infections

C E Friedgood and D B Ripstein (New York) remarked that urinary tract infections due to proteus have been completely refractory to all forms of therapy Furadantin, a new broad-spectrum antibacterial nitrofuran has been found to be effective against proteus A group of 92 patients with pyuria due to either cystitis or pyelonephritis were selected in whom the infecting organism was proteus They had all had intensive antibiotic therapy which was unsuccessful. The patients were then placed on divided oral furadantin therapy four times a day The acute cases showed a remarkable response to the drug with 90% cures within one week. The chronic group of cases had a lower cure rate of approximately 65% sterile urine cultures The only side reaction was nausea. There was no evidence of sensitisation.

Liver Factor in Cerebral Metabolism

A J Geiger and J Dobkin (Jerusalem) reported that the brain when perfused with simplified blood' consisting of well washed erythrocytes in albumin Ringer solution ceased to take up glucose and to oxidise carbohydrates, but regained these functions on addition of a liver extract After about 45 minutes of perfusion with simplified blood when the brain ceased to take up glucose an endogenous substance presumably not a carbohydrate, was utilised During an hour's perfusion the non protein nitrogen in the brain increased from 60 to 160 mg %, the amino N remaining around 40 mg % After an hour of perfusion mannose is easily taken up by the brain but not glucose 40 minutes of perfusion usually reduced the glucose content of the brain to 30% of the blood glucose concentration, suggesting that all the glucose was in the extracellular spaces During longer perfusion a further reduction of this relationship indicated the impermeability of the whole brain to glucose Lactic acid accumulated in the brain up to 300 mg %. Inclusion of the liver in the perfusion normalised the brain blood glucose relationship and reduced the lactate concentration Glucosamine added to the simplified blood was taken up by the brain at a rate of 3–4 mg per 100 g per min. at a concentration difference of 100 mg., even 60 min after the start of perfusion Part of the glucosamine was esterified in the brain. Its concentration in the blood diminished progressively indicating utilisation in the brain immediately after the addition of glucosamine Lactate diminished but increased again as more glucosamine was taken up

Myocardial Metabolism

W T Goodale (Boston, Mass.) R. E. Olson (Pittsburg) and D B Hackel (Cleveland Ohio) discussed contrasting patterns of myocardial metabolism in diabetes, in cardiac failure and after insulin administration in man. Previously reported coronary catheterisation studies in dogs and man have shown excellent correlation between myocardial respiratory quotient and myocardial carbohydrate utilisation. In mild diabetes, the fasting R.Q was 0 7 with markedly reduced or negligible myocardial glucose lactate and pyruvate extractions despite high circulating levels. The glucose utilisation threshold was elevated to 95–260 mg per 100 ml Insulin restored this threshold to normal or below with marked rises in R.Q to 1 1–1 2 and with normal or high utilisation of all three metabolites. These findings tended to confirm the rôle of insulin in converting carbohydrate to fat. Although diabetes caused defective myocardial carbohydrate utilisation there was no interference with mechanical work or efficiency Patients with cardiac failure due to valvular disease with reduced effective work and efficiency showed normal lactate and pyruvate and superabundant myocardial glucose extractions, relative to both arterial substrate levels and simultaneous oxygen extraction This unaccountable glucose extraction for non-oxidative purposes is also seen in myocardial tissue slices and other preparations with limited survival time There is no evidence for anaerobic glucose metabolism nor for myocardial lactate production in the failing heart in vivo Cardiac failure of this variety thus cannot be related to myocardial anoxia nor to a failure in energy production, but rather to a failure of conversion of chemical energy to effective mechanical work Paradoxically, the diabetic heart, with limited production of energy from carbohydrate even in mild cases, remains mechanically efficient with energy derived almost entirely from other substrates such as fat

Photography of Pelvic Organs

H. S **Guterman** and M R **Cohen** (Chicago) described a pelvic photoscope, developed by Dr Guterman, for the visualisation and photography of the surfaces of the structures of reproduction in the human female Colour photographs can be taken of anatomical changes observed in these structures during the menstrual cycle, and it is possible to correlate anatomical, physiological, and endocrinological changes in the same individual during a given time

Metachromatic Activity of Urine

L B **Jaques**, E **Napke**, and S W **Levy** (Saskatoon, Saskatchewan) had injected heparin in animals and man, and measured the metachromatic activity of the urine By quantitative precipitation of urine with benzidine, metachromatic activity equivalent to 2–13% of the heparin injected was recovered This contained an excretion product of heparin, uroheparin, with metachromatic activity and low antithrombic activity Following the injection of heparin, depending on the dose, the anticoagulant may be (1) destroyed by heparinase, (2) degraded to uroheparin, (3) excreted unchanged In the case of (2) and (3) metachromatic activity is found in the urine

Early Ontogenesis of Higher Nervous Activity

N I. **Kasatkin** (Moscow) said that an important way of investigating higher nervous activity in man is the study of its development in a child, beginning at the earliest age This method, together with the clinical method, is the most fruitful and makes it possible to follow the highly complex process of development of the main mechanisms of higher nervous activity, starting with its most elementary forms The advantage of studying the higher nervous activity during the first stages of the development of a child lies primarily in the fact that a newborn baby possesses only a limited fund of unconditioned activities. Subsequently, on the basis of unconditioned reflexes, very complex systems of conditioned reflexes are formed in a child, which in their turn influence and modify the unconditioned activity An experimental *investigation of the development of the higher* nervous activity in a child made necessary the elaboration of a method for its study A method of motor food, protective, and orientative conditioned reflexes has been worked out, on the basis of which conditioned reflexes from all analysers may be formed in a child during the first months of its life The appearance of the first conditioned reflexes indicates unambiguously that the activity of the cerebral cortex in a child has begun The formation of early conditioned reflexes obeys definite laws The first such reflexes to appear are noticed about the middle of the first month of life , the order in which conditioned reflexes appear depends on the analyser within whose limits they are formed , until the end of the first month of life conditioned reflexes, if they appear, are distinguished by their extreme instability The second month of the life of a child is an age when conditioned reflexes may be created within the limits of all main analysers A conditioned reflex, in the process of its formation passes through several stages In children born prematurely by one or two months, conditioned reflexes to auditory stimulation may be formed at the same age as in children born normally Ontogenetical investigation of the higher nervous activity of a child makes it possible to elucidate the most important laws governing the early ages of its development These laws, established by a strictly objective method, must form a sound physiological basis for the care and upbringing of small children

Cholesterol Metabolism and Diet

A **Keys** (Minneapolis) said that studies on physically healthy men on controlled experimental diets show that (1) addition or removal of dietary cholesterol is with effect on serum cholesterol , (2) serum cholesterol is u in severe calorie undernutrition , (3) serum-cholest increases during active weight gain, when only carbohy is added to the diet to produce overnutrition , (4) in balance, change in the proportion of calories supplied dietary fats produces parallel changes in the total cholesterol concentration in a few days, a new plateau established in a few weeks Both vegetable and an fats are effective Studies on population samples of phys healthy men habitually on diets differing in the propor of calories supplied by fats in England, Spain, Italy, and United States show

1 There is no important influence of dietary fat level serum-cholesterol from age 18 to the early 30s

2 There is an increasingly marked effect from the ea 30s into middle age 50 year old men on high fat di as in the U S A , have a mean serum cholesterol le some 50 mg per 100 ml higher than men of the same on diets where the dietary fats provide 20–25% of total calories, as in the general populations of Italy a Spain In upper class Spaniards on high fat diets t serum cholesterol is like that in the U S A

3 These population differences are not merely ref of total calories or relative obesity The Italians were fat as the American men and were fatter than the Engl men studied But calorie inadequacy combined with moderately low fat diet, as seen in poor Spaniards, associated with the lowest cholesterol values seen in age

4 There was no evidence for an effect of d cholesterol in these population comparisons. This with the finding in the U S.A that the individual cholesterol value is not correlated with habitual choles intake of the individual

Cortical Activities

P S **Kupalov** (Leningrad) said that the method conditioned reflexes permits a strictly objective physiolog study of simple nervous activity as well as of the most comp higher nervous activity which constitutes the normal na behaviour of animals The position of the animal in room becomes a positive conditioned stimulus if at moment when the animal occupies a definite place in the a stimulus is applied which has already become a c food stimulus After this when the experiment is repe the animal actively and spontaneously places itself in t very particular place of the room and all its motor acti becomes strictly determined Therefore there exist spa conditioned stimuli Experimental neuroses can be p even in such conditions when the behaviour of the is absolutely natural and the freedom of its motor acti is not hindered By combining different stimuli from environment, the motor activity of the animal, and the sp conditioned stimuli it is possible to work out a compl normal behaviour of the animal representing in itself unification of several conditioned reflexes into a single nerv activity Such complex conditioned reflexes have b designated "situation conditioned reflexes"

Drip-tube Feeding in Nephrosis

G T **Lewis** and J J **Griffitts** (Miami, Florida) d the effect of drip tube feeding on patients with n The material is administered by constant drip through plastic catheter inserted through the nose into the s or duodenum 3000 ml can be given in each 24-hour p and this provides protein split products equivalent to 1 of protein and approximately 3000 calories In nearly instance, œdema has disappeared within a few days follo the initiation of the régime and has not returned as lo the conditions were adhered to No claim is made that conditions responsible for the nephrotic state have corrected, but with this régime it is possible to mai the nephrotic patient indefinitely in a good nutritive and œdema free During this period, Nature has opportunity to correct the defect

Blood Coagulation

Jessica Lewis (Chapel Hill, North Carolina) dis prothrombin, proaccelerin, and proconvertin in coagulation Methods for the isolation of prot proconvertin, and proaccelerin from human plasma been developed, and the interaction of these mat e presence of tissue thromboplastin and calcium studied he methods employed in this study of isolated prothrombin oaccelerin, and proconvertin are also applicable to clinical stances of deficiencies of these coagulation factors. Thus e cause of a prolongation of the one stage prothrombin me (Quick test) can be readily identified if due to a ficiency of any of the three factors alone or in combination his is illustrated by representative tests on (a) congenital ypoproaccelerinæmia, (b) congenital hypoproconvertinæmia, d (c) mixed deficiencies associated with various clinical sease entities.

Ileostomal Steatorrhœa

D A. MacFadyen (Chicago) had obtained data from 4 bjects with surgical ileostomy on a standard analysed et for periods of four days each Fifteen months after a ior investigation under the same dietary and analytical nditions, one subject developed steatorrhœa with excretion 90–110 g of fat from an intake of 135 g The data show at calcium and phosphorus excretions were normal and e same on the occasion of steatorrhœa as on the earlier casion when there was no steatorrhœa The increase in tty-acid excretion about 45% of the total lipid excreted as accompanied by slight increases in excretion of potassium d magnesium and by a marked increase in sodium excretion om the usual amount of 50–75 m.eq a day to 110–150 m eq day The conclusion was drawn that under the conditions normal gastric secretion of hydrochloric acid and normal gestion of proteins, the digestion of fat in the small intestine accompanied after absorption of calcium chloride by rmation of sodium soaps and calcium phosphate sodium ing provided as bicarbonate from secretions into the testinal lumen according to the reaction $HA + NaHCO_3 =$ $aA + H_2CO_3$

Splanchnic Carbohydrate Balance

J D Myers, R F Kibler, W J Taylor L. W Hamrick L Engel, and E Werk (Durham North Carolina) said at the technique of hepatic venous catheterisation has lowed the measurement in unanæsthetised man, of hepatic nous glucose concentration. Thus the arterial hepatic nous glucose difference may be determined and when ultiplied by the corresponding hepatic blood flow which turn is estimated by bromsulphalein clearance the lanchnic glucose balance is obtained. In 60 control, sting human subjects, the arterial hepatic venous glucose fference was always negative and the splanchnic glucose oduction averaged 64 ± 3 1 mg per minute per sq m body-surface. Adrenaline pancreatic hyperglycæmic ctor and probably growth hormone all produce similar d prompt outpourings of glucose from the splanchnic ea with the production of hyperglycæmia Parenteral ucose abolishes splanchnic glucose output this effect is nulated by the response to small doses of insulin

Hypothermia

C. B Ripstein C E Friedgood and N Solomon rooklyn, New York) discussed hypothermia in cardiac rgery The production and maintenance of hypothermia s several applications in surgery At low body temperature e metabolic needs of tissue are greatly reduced and the art can be excluded from the circulation for fairly long riods without producing irreversible brain or cardiac mage The production of a controlled drop in temperature beneficial in hyperthermia accompanying severe sepsis, d the refrigeration technique has also been used to control tractable pain and to retard the growth of certain tumours. cent investigation has revealed that certain anti histamine ugs exert a thermoregulatory effect in warm blooded imals. One of these is dimethylaminopropyl N-chloro enothiazine HCl (Chlorpromazine) A technique of oducing hypothermia has been evolved using chlorpromazine conjunction with refrigeration blankets and cooling of the spired air With this method body temperature can be wered to 75–80 within 30–60 minutes, and the venæ cavæ n be clamped long enough to open the right atrium and close septal defect

Apocrine Sweat gland

W B Shelley and H J Hurley (Philadelphia) said that ere is a paucity of physiological data concerning the apocrine eat-gland in sharp contrast to the enormous body of owledge surrounding the eccrine sweat-gland. Recent perimental studies by them have indicated that the ocrine sweat gland activity may be divided into two phases: apocrine sweat secretion and apocrine sweating Ordinarily apocrine sweating is produced by emotional stimuli, but it may be readily induced by pharmacological measures (local or systemic adrenaline) or mechanical stimuli (stroking local pressure) Unlike the eccrine gland there is no response to acetylcholine and no inhibition by atropine In view of the fact that appropriate stimuli only empty the tiny apocrine gland and do not prompt any further secretion, the quantities of apocrine sweat which may appear on the skin at any given time are minute

Crystalline Glucagon

A Staub, L Sinn and O K. Behrens (Indianapolis) remarked that the hyperglycæmic activity first observable in certain pancreatic extracts and later found to accompany some insulin preparations has been termed glucagon by Murlin Recently they have been successful in isolating a unique crystalline substance from certain pancreatic materials The crystalline glucagon is unique in its high hyperglycæmic activity: 0 1 μg per kg administered intra venously to anæsthetised cats is sufficient to give a 30 mg rise in blood-sugar The properties of the crystals are sharply differentiated from those of insulin Crystallisation is in the isometric system the crystals appearing as well-defined dodecahedra Zinc is essentially absent Sulphur is present only to the extent of 0 6% and is accounted for largely by methionine Thus glucagon contains little or no cystine—an important component of insulin.

Nickel Metabolism

F W Sunderman and J F Kincaid (Philadelphia) discussed nickel metabolism following exposure to nickel carbonyl The concentrations of nickel in the blood and urine have been estimated in normal subjects and in individuals accidentally exposed to the fumes of nickel carbonyl. Administration of 2 3-dithiopropanol to critically ill subjects greatly increased the excretion of nickel in the urine For the prevention of acute poisoning the concentration of nickel carbonyl in air should be less than 3 parts per million for a period of less than 30 minutes.

Biochemical Abnormalities in Brain

D B Tower (Montreal) discussed biochemical abnormalities in epileptogenic cerebral cortex. It has been found that slices of epileptogenic cortex (sampled at operation on patients for focal cortical seizures) when incubated in bicarbonate-Ringer medium containing glucose and eserine fail to show the increase in their content of bound acetylcholine (ACh) observed in normal slices under these experimental conditions. This defect in ACh metabolism can be reproduced experimentally in slices of cortex from animals in which seizures have been induced by administration of methionine sulphoximine In none of these cases is there significant deviation from normal in production of free ACh. Addition of glutamine or asparagine (10 mM) to the incubation medium has been found to correct the impairment of ACh binding in each instance but has no effect on ACh metabolism in normal slices. When slices of cortex are incubated under conditions promoting normal ACh metabolism both the glutamine and glutamic acid content of the slices increase during incubation with no loss of either to the medium. With slices of epileptogenic cortex (human or animal) and with slices incubated under lowered oxygen tension the glutamic acid content of the slices fails to increase and glutamine may be lost to the medium during incubation. The addition of adenosine triphosphate (3 mM) or asparagine (10 mM) to the incubation medium under these circumstances will correct the defects in glutamine and glutamic acid metabolism.

Darmstoff

W Vogt (Frankfurt Germany) discussed *Darmstoff*—a smooth muscle-stimulating biogenic organic compound It was always found in the wall of the small intestine of all species under investigation, also in the stomach and the large intestine but hardly at all in skeletal muscle. It stimulates the intestine uterus, and bladder The action is not inhibited by atropine or ganglionic blockers *Darmstoff* is an acid, which in free form is only slightly soluble in water but is readily soluble in many organic solvents. Since it is not destroyed by trypsin there is no indication of a peptidic structure. By its acidic behaviour *Darmstoff* can be distinguished from choline, histamine and enteramine Bradykinin kallidin and substance P are different from *Darmstoff* as regards their being destroyed by trypsin Moreover, substance P is markedly basic in nature (according to their recent investigations) The only substance being an acid like *Darmstoff* is prostaglandin For the moment it is not known whether these two substances are related

Experimental Hypertension

G E WAKERLIN (Chicago) discussed treatment of experimental hypertension with renin and antirenin Chronic experimental renal hypertension in dogs has been successfully treated with crude and semi purified hog renins, and chronic experimental renal hypertension in dogs has been prevented by prophylaxis with crude and semi purified hog renins These therapeutic and prophylactic effects are well correlated with the antirenin titre This evidence of antirenin (or an antibody to a protein closely related to renin) as the mechanism of the antihypertensive effect of hog renin constitutes support for the primary rôle of renin (or some closely related protein) in the pathogenesis of experimental renal hypertension Spontaneous (essential ?) hypertension in the dog has been successfully treated with semi purified hog renin, the antihypertensive effect being well correlated with the antirenin titre Obviously, these findings are good evidence that this hypertension is on a renal, renin basis Since antirenin to hog renin does not neutralise monkey and human renins, studies aimed at altering the antigenicity of hog renin, so that the antirenin which it produces will neutralise monkey and human renin, are under way addition antirenin to human renin is being prepared goats and dogs, in order to study the possible pathoge rôle of the kidney in essential hypertension

Osmotic Pressure of Blood in Renal Papilla

H WIRZ (Basle) said that the kidney of the golden ha (*Mesocricetus auratus*) shows a long and thin papilla exte some millimetres beyond the hilus into the ureter part of the papilla can be exposed in vivo by dissecting ureter and part of the renal pelvis A quartz capi diameter 10–15 μ, was inserted in one of the papillary bl vessels, and small samples of blood (0 2–1 μg) were w drawn Immediately afterwards, equally small samples urine were collected from the tip of the papilla The fre points of both blood and urine were determined by a m cryoscopic method Urine concentrations ranged 0 30 osmol per litre up to 0 62 osmol per litre The osm pressure of the capillary blood was either the same or most, 0 03 osmol per litre higher than that of the c urine This indicates that the whole of the extrac fluid in the papilla is strongly hypertonic when the k produces a hypertonic urine The results give substa support to the theory, advanced by Wirz, Hargitay, Huhn, that a hairpin countercurrent system provided by loop of Henle is involved in the process of concentrating urine

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Special Articles

POLIOMYELITIS IN DENMARK
IMPRESSIONS FROM BLEGDAM HOSPITAL, COPENHAGEN

C A PALLIS
M.A B.M Oxfd, M R C P
SENIOR NEUROLOGICAL REGISTRAR, CARDIFF ROYAL INFIRMARY

THE 1952 poliomyelitis epidemic in Denmark, in which respiratory complications were prominent, has attracted much attention in this country, and many have visited Blegdam Hospital, Copenhagen, where Lassen [1] introluced the treatment of respiratory insufficiency by early racheotomy with insertion of a tightly fitting rubber uff tube, combined with bag ventilation, repeated aspiration and bronchoscopy, postural drainage, and the use of a stomach tube

At this hospital there remain a residue of "respiratory cripples," who provide dramatic proof of the severity of the outbreak In comparing the relative severity of different outbreaks of poliomyelitis, the number of cases requiring assistance with respiration in the acute stage is often misleading, since this gives no guide to the duration of the respiratory insufficiency A more precise guide might be obtained from the number of patients still requiring artificial respiration at various intervals after the acute illness, and this number would also give some idea of the amount of respiratory assistance required Such figures are available from Blegdam Hospital

WARD IMPRESSIONS

At this hospital chronic "respiratory" cases are nursed in a single block, in small wards with 3–8 beds Patients are transferred from isolation cubicles to this "chronic" block once the diagnosis is firmly established and the acute phase of the illness is over (The present policy is to perform tracheotomy, if judged necessary, while the patient is still in the isolation block, but at the height of the epidemic, when over 40 cases were being admitted daily, administrative niceties had to be waived and tracheotomy done wherever convenient) The patients usually remain in the "respiratory block" for several months In this block some patients are more or less amb others are totally tetra but all

require some help with breathing When the p are no longer in need of such help they are mo other parts of the hospital

The wards with chronic "respiratory" cases remarkable sight One is immediately struck by fact that, by day at least, they seem to contain ful many auxiliaries as patients The buildings are however, and nurses, relays of "ventilating" stude and physiotherapists do not seem to get in each way To each is assigned a precise function, and proceed methodically and with the quiet efficiency well established routine There is a constant noise from the asynchronous clicking and sighing mechanical positive-pressure respirators

In the acute stages of the disease a special nu detailed to each patient, but now each nurse copes with two, or sometimes three, patients One main duties is to deal with the secretions that accumulate in the larger bronchi The patients selves usually become quickly aware of these and localise them with remarkable accuracy Wheth rhonchus is palpable or not, the nurse vigorously p the appropriate part of the chest and immedi passes a suction catheter through the endotracheal or silver cannula The patients do not seem to mind and impressive amounts of secretion, that canno coughed up, are disposed of in this way This m may have to be repeated up to once an hour larger wards at least, one is sure always to see this applied to some patient or other

The nurse is often one of the first to recognise imp expansion of one part of the lung, and this is diately reported, if necessary verified radiographica and dealt with Anyone who has tried to d pulmonary collapse early, when the patient is nursed in a tank respirator, or who has struggled with problem of trying to examine radiographically patient (often capable, at most, of only a mini so of spontaneous breathing) will appreciate infinitely easier is this investigation when the pati "accessible" and when adequate ventilation maintained throughout My recollection of such tions when the patient was not accessible in this is that they were often veritable nightmares The had to be disengaged if the patient was to be over and the lung bases examined The exam commonly had to be extremely cursory, and the total ventilation often made it difficult to detect of diminished air entry Positioning of radiogr ates and centring of tubes were likewise hurried and en erratic. Occasionally the patient would go black the course of the examination and have to be ecipitately restored to the tank.

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[1] ssen. H

With the new method the treatment of pressure ints is also much easier, for the back can be attended often and thoroughly I saw next to no bedsores at egdam Hospital even though many patients were tally tetraplegic and some were but skin and bone chnically, this is a remarkable achievement This all in striking contrast to the chaotic few minutes ring which the severely affected patient can be kept t of a tank respirator then the back may have to be tended to at the same time as another nurse is adminis ring an enema or giving an injection, and while the octor is attempting to examine the patient

Each patient receives physiotherapy repeatedly roughout the day Hot packs are applied even in ronic cases, before putting joints through their full nge of passive movements. Significant contracture is re even in patients tetraplegic for nearly a year The ght of totally wasted limbs some showing vasomotor ralyses, quite free of contracture was new to me This a triumph which reflects both the thoroughness of the ysiotherapist and the accessibility ' of the patient

Certain changes in the technique originally described Professor Lassen have been introduced over the past w months Air is gradually replacing the original ygen nitrogen mixtures open-circuit methods with rious ingenious types of expiratory valve are taking e place of the closed circuits with their soda lime nisters; and ventilation is now carried out at least often mechanically as by relays of students The ajority of patients I spoke to who had had experience both methods, preferred the machine —particu rly at night On the other hand most patients had eferred the students in the early stages of their sease when respiratory paralysis was complete morale ther shaky and fear of the implications of engine- ouble' very real. Some patients preferred the students r conversational reasons Some students were sociable mpanions others had mastered the technique of multaneous study and ventilation

There is a certain amount of misconception about the atient s ability to speak when treated by the Copenhagen ethod. The endotracheal tube is passed through a acheostomy and is therefore not in contact with the ocal cords It can be kept in this position much longer an when it is passed through the larynx without fear causing ulceration of the mucous membranes During e phase of bulbar palsy the air-cuff is kept blown up d thus acts as a hermetic seal, isolating the oropharynx om the trachea. Saliva cannot drown the patient ut neither can air pass up the other way and phonation therefore impossible This is only a transient phase owever most patients with bulbar palsy either die uickly or else recover soon Chronic bulbar palsy was ardly seen at all. Some patients retain the cuffed be (changed as necessary) for up to six weeks but the ajority for shorter periods. Once the patient can allow again the cuffed rubber tube is replaced by a lver tracheotomy cannula The patient can then eak intelligibly This is a big step forward and all o patients spoken to commented on the profound ychological effect it had had on them Other notable ates for the patient are those of the removal of the acheotomy cannula, the discontinuation of assisted uirasse) breathing and finally discharge from the respiratory block The various phases of rehabilita- on are somewhat reminiscent of the graduated régime a well run sanatorium

The atmosphere of the wards was one of genuine good eer with picture books and toys in the children s ards and games of chess, wireless and so on in the wards for adults Wards containing two or more Both respirators readily assume a sinister appearance but there was none of this here

RESIDUAL RESPIRATORY DISABILITIES

321 cases of poliomyelitis with respiratory trouble of one type or another were admitted to Blegdam Hospital following the adoption, late in August 1952 of the new method of tracheotomy and positive-pressure intratracheal ventilation; the vast majority were admitted during the months of September and October Of these patients 202 survived. 57% of the survivors still required assistance with breathing after a week, 40% after a month 28% after three months and about 20% after six months At the end of July 1953 29 patients (14% of the original 202) still required whole-time or part time artificial respiration One fact immediately emerges from these figures—that 'respiratory recoveries' are still occurring I was shown a case in which repeated fluoroscopy had shown paradoxical diaphragmatic movement for nearly six months after the onset of paralysis and where normal movements were beginning

Careful daily charts are kept of the maximum duration of continuous unassisted breathing each patient is capable of and also of the number of such attempts he is prepared to make in each twenty four hour period Many of the charts reveal delayed recoveries some partial, others more complete The patterns of respiratory recovery are varied. In some cases the duration of individual bouts of unassisted breathing slowly increases in others the patient gradually becomes capable of many more such bouts each day without significant change in the duration of each individual attempt

These facts challenge many widely prevalent views. If as the Danish figures suggest recovery of a diaphragm paralysed for several weeks is by no means exceptional then every effort must be made to keep the patient free of bedsores and contractures for as long as possible I have mentioned the success of the Danish methods in this respect. Perhaps we used to feel over here that contractures and bedsores were not fundamentally important, when the only prospect was several months in a tank respirator culminating in the merciful release of a terminal bronchopneumonia It may be argued that at Blegdam Hospital much intensive physiotherapy and nursing was 'wasted on some of the more hopeless cases. (This is a serious ethical problem of which our Danish colleagues are well aware) Other patients, however with less severely affected limbs, have without doubt benefited by the new method for when breathing returned, their limbs were in fair condition Few patients emerge from a tank respirator, after six months or more in a condition anything like as good as that of the Blegdam Hospital patients when their cannulæ are finally removed

29 patients still need ventilation There is clear gradation of respiratory crippling from very severe to minor requiring only a little help to ensure a peaceful night several of these patients are about to be "weaned ' Of the patients who had been in the block for more than six months 8 were incapable of even thirty minutes continuous unassisted breathing a further 8 could cope with periods of half an hour to five hours; and 13 managed spans of two or more hours The ' total spontaneous breathing time' per twenty four hour period showed a similar scatter 9 patients achieved summated breathing times of less than half an hour 9 times of one to twelve hours and 11 times of more than twelve hours

In these 29 cases associated paralyses were severe and at least 17 of the patients were tetraplegic. 'Tetraplegia here denotes not merely that a few muscle groups have been paralysed in each limb but that almost every anterior horn cell—from the upper cervical seg ments to the lower sacral—had been severely affected In many of these cases there is paralysis of the neck muscles with a "floppy head," severe diaphragmatic and intercostal paralysis, and paralysis of the dorsal and abdominal trunk muscles, in addition to virtually total paralysis of both arms and of both legs In the early stages many of these cases also had paralytic ileus and retention of urine I attended a necropsy of one such case, and the spinal cord and anterior roots showed a most striking appearance, there were no stones in the kidneys, and the lungs showed no gross changes The histological material accumulated at Blegdam Hospital in the course of the past few months promises to be most instructive

Of the 27 patients in hospital for seven months or more, 4 had proved renal calculi, 1 probably had calculus, 1 had an infected bladder and 1 had had hæmaturia Thus 7 (just under 25%) of this group of patients had urinary complications This is presumably the price of prolonged immobilisation, though it is difficult to see how it could have been avoided. Pathological fractures have occurred in 2 patients

My thanks are due to Dr J D Spillane for his help in arranging this visit, and to Prof H C A Lassen for his permission to comment on the patients under his care I should also like to thank the staff at Blegdam Hospital for their helpfulness

Medicine and the Law

Dentist and Anæsthetist

ON questions of professional liability to patients the Ministry of Health neither has nor professes to have any authority to declare the law It can, however, give guidance as advised by its legal staff

At a meeting on Sept 24 London Executive Council heard the Ministry's comments on a case in which the dental service committee had reported its opinion that there had been an unavoidable breach of a dentist's terms of service in connection with the administration of a general anæsthetic Although the fault lay primarily with the anæsthetist, the responsibility for the treatment of the patient nevertheless rested with the respondent dentist against whom a complaint had been made The dentist offered to forgo the fee paid to him in respect of an upper denture The dental service committee recommended that the offer be accepted, the executive council agreed and so also did the Ministry of Health to whom the report was communicated The Ministry, however, disagreed with the finding that there had been a breach of the terms of service "The Minister," it stated, "is advised by his lawyers that under the regulations the dentist is not responsible for the acts and omissions of the anæsthetist, and that any person who suffers injury at the hands of the anæsthetist should be left to his civil rights for a remedy"

The Ministry's statement appears to be right and reasonable Why should a dentist, any more than a surgeon, be responsible for what the anæsthetist does or does not do?

Transfer of Girl from Mental Hospital

The handling by the Home Office of the case of a 14 year old girl who has spent a year, latterly as a voluntary patient, at Hollymoor Mental Hospital, Birmingham has been sharply criticised by the chairman of the hospital management committee[1]

Last year the girl was found by a juvenile court to be in need of care and protection Five men were convicted of offences against her Last October, when she was said to have developed suicidal tendencies, she was transferred to Hollymoor Hospital from a remand home

In a statement issued on behalf of the hospital management committee, Mr. David Rhydderch, the ch said that the hospital authorities were informed on the morning of Sept 22 that the Home Office intended transfer the girl to Shore Hill Classification Sch Warrington, on Sept 28 On Sept 23, however, the g father gave the statutory three days' notice that intended to remove the girl from the hospital The n day the juvenile court amended the original approv school order, bringing forward the date of transfer Sept 25 Mr. Rhydderch said

> "It may be asked where was the need for such comp synchronised timing arrangements We have a str feeling that this was necessary in order to avoid embarrassing consequences of the legal blunder made wh parental authority was reconferred We deplore t indifference and the neglect of the Home Office author which allowed this young girl to remain almost 12 among adult mental cases, in spite of repeated lette pleading for her transfer We also say that to transfer girl to a place as distant as Warrington is far from fair to t parents, who will be unable to visit because of the dist and expense of travel"

In a statement issued last Tuesday, the Home Off explained that this case had been under considerat since last April, when on medical advice measures w taken to secure the girl's transfer to an institution mental defectives By the end of August no vacan in an institution for mental defectives had been found the regional board, and in view of representatio the chairman of the Hollymoor Hospital Managem Committee and others, the case was reviewed In co quence the girl had been transferred to Warrington observation The statement pointed out that an or made in September, 1952, for the girl's detention Newfield School was still in force, but this had to endorsed for the Shaw School, Warrington

Public Health

Poliomyelitis

POLIOMYELITIS notifications (uncorrected) in Engl and Wales during the week ended Sept 19 (37th w of the year) were as follows paralytic 123 (92), n paralytic 104 (81), total 227 (173) This is an incre of 54 compared with the previous week, the figures which are in parentheses

This increase is largely accounted for by an increase notifications of 15 in Coventry and 14 in Kettering, both places there has been an abnormally high inc of the disease

Second Quarter in Scotland

In the three months ended, June 30 this year, birth-rate in Scotland[1] was 18 0 per 1000 popn which is 0 1 more than the rate for the co quarter of 1952 The number of stillbirths was equival to a rate of 24 per 1000 total births The death-rate in the corresponding quarter of 1952, was 11 2 per 1 population The infant-mortality rate was 29 per 1 live births, this rate is 5 below that for the c quarter of 1952, and is the lowest recorded for a quarter The death-rate from tuberculosis was (respiratory 22) per 100,000 population The former is 6 less than that for the corresponding quarter of 19 and the latter is 3 less, and these rates are 32 and below the five years' average

Fertility in 1931 and 1939

The last volume[2] in the series of decennial supplem to be issued in connection with the Census of 1931, published, analyses data on fertility in that year and 1939

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[1] *Times and Manchester Guardian* Sept 26 1953

[1] Quarterly Return of the Registrar-General Scotland B Deaths and Marriages registered in the quarter ended 30th J 1953 H M Stationery Office Pp 30 2s 6d

[2] The Registrar General's Decennial Supplement, England Wales 1931 Part IIB Occupational Fertility, 1931 and H.M Stationery Office Pp 99 13s 6d.

In England Now

Running Commentary by Peripatetic Correspondents

IT is probably true that the activities of Mr William Illott have been on balance *beneficial to the country* nt in at least one household they have left a legacy of onfusion and despair We can never find the paragraph the papers which tells us whether to put the clocks rward or back and if we once falter in our empirical elief and sit down to argue the matter out we are retrievably lost. In fact, we have to get up unreasonbly early on Sunday morning to find out from the .B C whether or not we are two hours wrong

All this is of course, child s play to the Americans o recently attempted a journey by rail from Cincinnati Chicago, where we were to catch a plane We were esh and fit when we reached the travel agency and we ad a little notebook to take it all down in It was not ll we were immersed in schedules that we realised we ere travelling on the day summer-time reached Chicago ut not Cincinnati The young lady was most helpful e would leave Cincinnati on Eastern Standard Time ut at Chicago we would be on Central Standard Time that normally we would have to put our watch back n hour But then' she said, Chicago will be on ummer time, so you ll have to put it right on again ' Ve were immediately roused 'Well then we said *what time is the time we are due to arrive in Chicago* ritten in? Central Standard I guess said the oung lady doubtfully ' I don t know much about trains yself. She rummaged in the back of the schedule Yes, she said 'Central Standard So' we said raftily the train journey will actually take an hour onger than we think it will—or will it? The young dy smiled patiently You won t have to alter your atch, will you?' she said speaking slowly and dis inctly No, we replied thankfully 'Well then he said it will be an hour later than that time on our watch' 'We see' we said slowly (we really hought we did) "Then how long will we have in hicago till the plane leaves?' Ah, said the young dy in a businesslike fashion, ' planes are different. Ve'll have to see what time your airline is operating on Vhere did you say you were going?' We told her and he had begun to look it up when a thought struck her They'll be on Mountain Time, you know, she said and that means you'll have to put your watch back wo hours instead of one before you get there Unless, f course they're having summer time too

We staggered out our spirit broken. When the time ame we *turned up an hour too soon* at Cincinnati

* * *

We have just acquired a puppy of tender age and he as been installed in a box in the kitchen. The first w nights we had him he cried like a baby and refused bo comforted until he was taken upstairs and allowed crawl under the bedclothes of one of the junior members the household He wasn t cold he wasn't hungry he st wanted company in bed with him But we did not ceive an expensive physiological education for nothing, nd we have rigged him up a heart-lung preparation in s box for him to sleep with. It consists of a rubber ot water bottle on top of a ticking alarm-clock, and he eeps like the dead.

* * *

We thought that what was good enough for T E. awrence would be good enough for us, so the prepara ons for the expedition were put in hand and one sunny y we set out to follow the master s *footsteps* We chose canoe that was narrow and light—Canadian pattern o were told and rather unstable for the novice

The river was low and the current sluggish it being e hot season and we were able to make the upstream urney at a fast pace the canoe handling beautifully e had however to turn up a narrow tributary to the ght and were soon in the shallows and then completely ounded Stepping out into the now rapid current we uled the boat up over the flat stones into deeper iner water again and then paddled on ducking our ads to avoid the overhanging vegetation which by w almost closed over the whole width of the stream ll was still and as we rested on our paddles the silence seemed to close in on us and it was a relief to hear the splash of the water again Rounding a last bend to the right we found ourselves at the mouth of the tunnel which we found to be blocked by underwater debris over which the craft had to be carried Once this obstacle was passed we found to our relief that we were in deep water again. After about twenty yards the tunnel turned sharply to the left and we were in complete darkness soon to be pierced by the light of our torches. The walls of the tunnel were covered by a slippery brown alluvium but the air was cool and sweet and we made rapid progress. Faintly in the distance we heard the silvery tinkle of a small waterfall which seemed to call *us mysteriously on. But suddenly* with a *spine-chilling* scraping sound the canoe grounded We stepped out with some difficulty and pulled the boat forward into deep water again but on attempting to regain our seats we misjudged the slippery floor and the instability of the craft the latter turning over sinking and precipitating us completely into the black water Cushions socks shoes, paddles began to float away and we retrieved them with difficulty But the worst task was to raise the dead weight of the boat and hold it up over our heads to empty it. In the confined space the water poured all over us and when we finally sat down again we squelched miserably Thrice more we were grounded as the tunnel wound its sinuous way and the roof became alarmingly low However, we had learned how to get in and out of the canoe without tipping it over and the first horrifying mishap was not repeated We saw no animal life larger than small water-snails which covered the walls in great numbers and whose sharp-pointed shells were painful to the feet

After turning a last bend to the right we saw the bright light streaming through the exit ahead, and shooting through a hanging fringe of ivy leaved toadflax we were *out in the warm sunlight* and *scented air of the water* meadow The narrow canalised stream continued on between high banks overhung by dense bushes and trees and then suddenly widened out and entered the main river bringing us back to the streets of the town which we had toured by underground waterway

We were somewhat disappointed by the expedition Lawrence wrote of fast-rushing water gates closing the exit of the tunnel and the danger of being trapped by a sudden rise of water Maybe he chose the wrong season for his trip we certainly did—another six inches of water and we would have come through without mishap The obstacles which had been our undoing were piles of stones and bricks thrown down the inspection holes normally covered by heavy iron lids. It was up these same inspection shafts that Lawrence had discharged his revolver maybe the bricks and stones indicate retaliation by the surprised citizens of that time

The boatman seemed surprised at the water in the canoe until we told him that we had capsized I told you it was a wobbly one he said We could not but agree

* * *

Once again I ve got to face it. I haven't seen a child with a fish hook in its finger for a fortnight. The spate of Temporary Residents complaining of sunburn sand in ears and summer-diarrhœa is easing off. The Follies on the Parade have folded their tents. The shops are full of winter clothes fur lined gloves, and warm bootees Summer dresses are disappearing from the Front and swimming-suits are no longer there My spare time is occupied with bonfires of swept-up leaves. My nine November maternity cases, booked so lightheartedly in the early spring loom alarmingly near Patients cluster round for their anti-catarrhal vaccine; one even proudly displays her first crop of chilblains. I ve tried to ignore it, but winter will soon be here: the evenings are drawing in and as usual I don t like it.

* * *

To protect my consulting-suit during the washing up the children gave me an apron for my birthday It is a great success but I tend to keep away from windows, and feel that it might have been more appropriate for one of my surgical colleagues It is navy blue with white vertical stripes.

* * *

How Do I Treat My Doctor?
Very seldom.

Letters to the Editor

THE R M B F

SIR,—I shall be most grateful if you will spare space in your columns for me to appeal for donations to the Royal Medical Benevolent Fund to enable us to distribute Christmas gifts to beneficiaries of the fund

I hope that all members of the profession will contribute towards this extra help at Christmas time, for it is enormously appreciated by doctors and their dependants who have *fallen on hard times* The fact that they are remembered by their more fortunate colleagues gives the recipients of gifts even greater pleasure than the gifts themselves, which, however, provide extra comforts or small luxuries for which they have been longing

I ask subscribers to the Fund to spare a little more for this special purpose, and I beg others to become subscribers at the same time as they respond to my present appeal

Donations and subscriptions should be sent to the Secretary of the Royal Medical Benevolent Fund, 1, Balliol House, Manor Fields, Putney, London, S W 15, and marked "Christmas Gifts"

WEBB JOHNSON
President,
Royal Medical Benevolent Fund.

PREVENTION OF POLIOMYELITIS

SIR,—I have been very interested in the discussion in your columns following Dr Agerholm's stimulating article (Aug 8)

I agree wholeheartedly with her views on prevention of spread and necessary quarantine—although at present such measures cannot be fully applied except to school children, teachers, and food-handlers A great deal can be done by discouraging unnecessary movement of people from an infected area Every additional week that the disease is contained in a locality is a great gain in view of the comparatively short season of poliomyelitis.

Dr Agerholm's hypothesis that changes in the epidemiology of the disease are due to the recent importation of an immunogenically new virus deserves careful consideration She makes two main points in favour of this hypothesis

1 "The age incidence has altered " But this is no recent change, as is shown by the following extract from the annual report for 1911 of the medical officer of health for Cornwall "the disease has obviously changed its incidence, the average age of 50 consecutive cases being 6 years, which appears to be high for infantile paralysis even adults now frequently succumb to the disease"

2 "The proportion of symptomless infections appears to be greatly reduced, and multiple cases in a family or school have become relatively common" I assume that symptomless infections here means non paralytic cases

My experience in Cornwall has been that the ratio of paralytic to non-paralytic cases has varied in different years In 1947, and again in the present year, there has been a high proportion of non-paralytic cases, and of the paralytic cases few have been really severe, whereas in 1949 and 1950, when the incidence in the county was heavy, there was a high proportion of severe paralytic cases

Such a variation might well be due, as Dr Agerholm suggests, to a different virus being present in severe epidemic years I am uncertain whether there has been any increase in multiple cases of recent years The difficulty is that few outbreaks before 1946 were adequately documented, indeed, for much of our information we must return to the 1911 outbreak In this outbreak, Reece tells us (*Rep loc Govt Bd publ Hlth,* 1912), amongst the 154 cases which occurred in Devon and Cornwall, "in four instances there were two cases, in two there were three cases, in four there were f cases and in one instance, there were six cases in a hous It is evident, therefore, that the changes at pre apparent in the epidemiology of the disease have occur gradually and cannot be cited in support of the hypoth of the recent introduction of a new strain of virus.

Truro Cornwall E R HARGREAVE

SIR,—In the Silver Blaze mystery the pivotal fact Sherlock Holmes's mind was that the dog did not in the night, a negative clue in the mystery of incidence of poliomyelitis I suggest that attention has not been paid to the people who exposed to infection and do not get the disease. rural practitioners are familiar with the phenomenon two or three cases of poliomyelitis (or more comm of infective hepatitis) occurring in the same parish no obvious point of contact between them something remote like the handle of the village p office door or contact with a contact of a contact, are irresistibly forced to the conclusion that is widespread and susceptibles are rare. Indeed, several regions of the U S A four-fifths of the over 14 years of age were found to possess poliomye antibodies Bearing in mind the prodigious habits of viruses, the country general practitio realises that with one case in the village it is as if population of China had erupted into Lower Snor which makes Dr Agerholm's suggestion of herds of contacts a little impracticable But why not everyone get poliomyelitis? Individual resist the virulence of the organism, chance? From meagre experience in wandering round as a tenens I have a hunch that the main element in mining immunity is the presence of another virus protects the host, a jealous virus, sometimes strongly, sometimes weakly, the well-known faculty or gift for "interference" May I the scraps of experience that have led me to this

1 In the Auckland, New Zealand, epidemic years ago I was shown cases by Dr Sweet, the child specialist, who gloomily admitted that the disease was his Truby King fed children, his excessively hygienic babies

2 A boy of 11 in the junior school, attached to a public school, whose housemaster's baby had been sent to hospital with poliomyelitis the week before and the boy had actually touched, had a febrile illness pain in the neck as no 1 symptom for ten days. The spec said it was not poliomyelitis, on the insufficient ground there was no muscular weakness, but, of course, it But why did not his younger brother or some other at the school who must have been infected get any This is an ordinary experience, a textbook example of capricious incidence of poliomyelitis

3 I saw a youth of 19 in a Norfolk village who in of sore throats complained of sore throat On my visit he diagnosed himself "I am much better, but I lift my left arm" A few days later, a mile away and no obvious connection with this case, I saw a woman alone in an isolated house with three young children, two whom were on her bed Her chief complaint was pain the back, following "flu" I wired for her husband who on service and got the M O H to see her He was doubt but next morning before breakfast there was no doubt all She was sent to hospital where, tragically, she few days later in an "iron lung" But why did those ch escape? There can be no doubt about the virulence of organism here

4 In another county I was shown a girl who in a epidemic of poliomyelitis thought she had the disease, was labelled as "neurotic" on the somewhat ground that her brother was in a mental hospital. I measured her up and found she had muscular wasting sent her off for treatment This girl had limped a mile to see some friends or relations who had five small and I was called to see these, one after another, with peratures, pains in the back and legs, vomiting, and meningism all of which passed off in twenty four

ıg up the M O H but he seemed reluctant to play ball the idea that there could be five cases of poliomyelitis ıo household and being only a locum I let it pass. But could possibly be the deciding factor which allowed group of children to be infected and another group with ser contact with a known case to be spared ?

suggest that some very rewarding information ıt be gathered—especially by the field naturalists of icine, the rural practitioners—by inquiring into what mon virus diseases people who get poliomyelitis not had and close contacts who do not get it had Personally my guess is that the villain or or hero of the piece is herpes simplex It is the most spread viral infection in man It is contracted in childhood and is kept as a slightly irritable pet ughout life Adults do not get it but, of course periodically display their childhood s infestation ıet and Williams found that 93% of hospital patients antibody in their blood but only 37% of the more enically brought up university graduates Over are infected and remain carriers for life' says of the authors of that mine of information *Virus Rickettsial Disease* In short I suspect that herpes lex negatives are liable to become poliomyelitis s. I suggest that there is a prima facie case for stigation, which I understand has not been made in words that Holmes himself might have used us herpes simplex follow, my dear Watson, may be man.'

ckley Rye, Sussex. C G LEAROYD

TRANSFUSION OF BLOOD PLATELETS

R —I think that your leading article on this subject t 19) calls for comment for the sake of full correctness r concern about cerebral hæmorrhage in idiopathic mbocytopenic purpura is a bit theoretical. The lence of cerebral hæmorrhage in this condition is —probably very low During the past fifteen years ıve personally followed up 20 cases these have ıded some with profuse bleeding but none with bral hæmorrhage This is perhaps a small number irm conclusions, but as personal series go it is quite

ou state that commonly acute idiopathic thrombo penic purpura is clinically severe and responds poorly plenectomy ' The first part of this statement may rue but the second part does not harmonise with rience in this part of the world In my series, t of 14 cases had to be splenectomised immediately ıg to profuse bleeding Of these patients 1 died hrombosis and subphrenic abscess some time after nectomy *the rest are fully cured*

egarding transfusion of platelets before splenectomy ny experience ordinary transfusion of fresh blood re or during splenectomy has a satisfactory effect r the splenic vessels have been ligated, the remaining ding tendency disappears remarkably soon

Joseph's Hospital
orsgrunn Norway

A SCHRUMPF
Chief physician

TOBACCO SMOKING

R,—I should be grateful if you would allow me space hange the middle of the definition of addiction given ıy letter last week from tolerance to the physical ts of the incorporation on the basic psychic relations ı to read tolerance to the physical effects ıe incorporation the basic psychic relations with

otts Lanarkshire R GOOD

IR,—Dr Good offers us a twelve line definition of iction Might I with very great respect suggest he should read what he has written aloud ?

ughton, Essex. ALEX COMFORT

URINARY EXCRETION OF CITRATE

SIR,—The interesting preliminary communication last week by Dr Fourman and Dr Robinson shows that a decrease of urinary citrate clearance may be associated with experimental potassium depletion in man but there is no definite proof that this is directly due to the potassium loss The clearance of citrate by the kidney is a very complex process since urinary citrate as measured chemically consists of at least three different fractions—i e. dissociated citrate anions balanced by sodium or potassium, undissociated citric acid itself and un ionised calcium citrate chelation complex. Gamble[1] has shown that the degree of dissociation is governed by the urinary pH and Hastings et al[2] have studied the effect of citrate as a calcium chelating agent. As will be seen there is reason to believe that these three moieties are handled differently by the renal tubules

The renal clearance of citrate is greatly modified by at least five distinct factors (*a*) plasma level of citrate, (*b*) pH of the urine (*c*) calcium content of the urine (*d*) œstrogenic and androgenic steroids, and (*e*) presence of urinary infection

(*a*) Like most other substances reabsorbed by the tubules from the glomerular filtrate the citrate clearance increases with rising plasma levels

(*b*) Free citric acid appears to be reabsorbed preferentially to citrate ion, and therefore the citrate clearance increases as the urinary pH rises.[3, 4]

(*c*) Calcium citrate chelation complex is less well reabsorbed and therefore the citrate clearance increases with a rise of urinary calcium[5]

(*d*) Œstrogens specifically increase and androgens decrease the renal citrate clearance by a direct action on the renal tubules[4] This is of little practical importance in the male but accounts for the wide cyclical fluctuation of citrate excretion in the female during the menstrual cycle[6]

(*e*) Urinary infection diminishes citrate clearance since citrate is rapidly destroyed by many bacteria in the bladder and the renal pelves as well as in stored urine[7]

In the course of an investigation on calcium metabolism,[8] all these facts were confirmed but no new information was elicited In the data presented by Fourman and Robinson it seems that the effect of variation of calcium content of the urine may have some bearing on the fall of citrate clearance observed It is virtually impossible to produce an absolutely pure uncomplicated potassium depletion in man In the method described by Fourman[9] there is a complicating acidosis due to the use of a sulphonic resin in the ammonium cycle and also there is preferential absorption by resin of divalent cations in the gut with a consequent reduction in calcium and magnesium intake Hypocalcæmia and tetany have been reported after relatively short periods of therapy with the sulphonic forms of cation exchangers[10] and urinary calcium usually drops very rapidly with ingestion of such resins In experimental potassium depletion studied by Black and Milne[11]

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1 Gamble, J L. Chemical Anatomy Physiology and Pathology of Extracellular Fluid. Cambridge, Mass. 1951 chart 20
2 Hastings A B., McLean F C., Eichelberger L. Hall J L. da Costa, E. *J biol Chem.* 1934 107 351
3 Östberg O *Skand. Arch. Physiol* 1931 62 81
4 Shorr E, Carter, A C., Smith, R W jun., Tausky H Macy Foundation Conference on Metabolic Aspects of Convalescence New York 1948; 17th meeting
5 Shorr E., Almy, T P., Sloan M. H., Taussky H Toscani V *Science* 1942, 96 587
6 Shorr E., Bernheim, A R., Taussky H *Ibid*, 194? 95 606
7 Conway N S., Maitland, A I. L., Rennie J B *Brit. J Urol* 1949 21 30
8 Milne M. D M D thesis Victoria University of Manchester 1951
9 Fourman P *Lancet* 1952 i 1012.
10 Greenman L. Shaler J B., Danowski T S *Amer J Med* 1953 14 391
11 Black, D A. K., Milne M. D *Clin Sci* 1952 ii 397

which differed from the method of Fourman in that a resin in the sodium cycle was used in the pre treatment of the diet, the calcium content of my own urine dropped sharply from 53 to 5 m eq per day during the depletion period I have confirmed the correlation between calcium and citrate excretion in my own case,[8] the correlation coefficient being $+ 0.92$ at ordinary urinary pH range The regression equation of citrate to calcium was of the formula $y = 0.85x + 0.2$ where y is citrate excretion in mg per minute and x is calcium excretion in the same units It is probable that the regression constants vary considerably from individual to individual Applying these results to the data on potassium depletion, I would have expected a fall of citrate excretion from 1180 mg per day to 370 mg per day *due to the effect of hypocalcuria alone* This is a greater fall than that recorded by Fourman and Robinson, but it must be admitted that the high-milk diet of our depletion experiment caused an abnormally high calcium excretion during the control period Studies of citrate excretion will in future be included in a research on potassium depletion at present in progress in these laboratories

If it is finally shown that potassium depletion has a direct effect on citrate clearance, it is still difficult to agree with Fourman and Robinson that this would probably be secondary to abnormal glucose metabolism with disturbance of the metabolic processes of the tricarboxylic acid cycle This should influence citrate clearance rather by alteration of plasma citrate levels than by a direct action on the kidney The publication in full of the data of Fourman and Robinson, with details of the effect of variations of calcium excretion, will be awaited with great interest

Postgraduate Medical School
of London W 12

M D MILNE

EXTERNAL CEPHALIC VERSION

SIR,—In reply to Mr Dalley's letter (Sept 12), I wish to point out that the two sets of figures he analyses are not comparable In forecasting the probable outcome of 1000 cases of breech presentation diagnosed during the course of pregnancy in the Middlesex Hospital, he forgets the number of successful versions which would result from version without anæsthesia, and it is in 80% of the remainder that version would be likely to succeed with the help of anæsthesia Thus the total number of cases in which version as a whole is likely to prove successful is necessarily much more than 80%, and will undoubtedly reduce the incidence of breech presentation in labour well below the 60 per 1000 estimated by Mr Dalley In fact our incidence of breech presentation in babies weighing more than 3.3 lb at birth was slightly below 16 per 1000 (corrected figure)

Middlesex Hospital,
London W 1

M R FELL

ACROPARÆSTHESIÆ IN THE CARPAL-TUNNEL SYNDROME

SIR,—I was very interested in the article on this subject by Dr Kremer and his colleagues (Sept 19), as I have dealt with quite a number of these cases by operation The procedure adopted by me has, however, been a more extensive exploration through a vertical incision, which included examination of the flexor tendons and their sheath as well as the flexor retinaculum The vertical incision has never caused any contracture, and the median nerve has never become adherent to the scar

With this more extensive exploration the flexor tendons are seen to be enveloped in œdematous synovial membrane, this œdema, which is often severe, resembles, though it is more extensive than, that seen in tenovaginitis stenosans of the short extensor and long abductor tendons of the thumb I contend that this condition called acroparæsthesiæ in the carpal-tu syndrome is a tenovaginitis stenosans involving flexor tendons as they pass under the flexor retinac In this particular instance, it is complicated b passage of the median nerve through the same tu the tendons The nerve, being the more delicate ture, gives rise to earlier and distinct symptoms.

The treatment is the same as for tenovaginitis sten elsewhere—i e , division of the tight constr band

Norwich

G K McKe

"COIN" LESIONS OF THE LUNGS

SIR,—Your annotation of Sept 19 indicates the r which any person who "believes himself to be in health" may run if he submits himself to mass graphy, for it tells us that if his radiograph show shadow of a small healed localised lesion he ma induced to submit in turn to multiple radiogra examinations, tomography, angiocardiography, r active isotopes, bronchoscopy, and biopsy

"When all these investigations have been comp however, the answer is very often still in doubt The place for these lesions is in the hands of the pathologist it is probably wiser to remove them all, tuberculous and tuberculous, except perhaps in patients under the age o in whom the shadow lies at the apex of a lobe"

On this principle would it not be logical to rem lung as soon as you see a shadow on the radiog This would surely save our overworked radiolo biochemists, pathologists, anæsthetists, and all technical and nursing staffs—yes and the a great deal of labour Speaking of the alternative p of "waiting, watching, and operating only if the enlarges or excavates," you say that "in view of safety of modern surgery this course is s justified" Is even anæsthesia always administ without risk?

In Storey et al 's series, of 40 patients (mostly h young men on active service) in whom a histo diagnosis was made, the lesion proved to be tuberc in 70% As a radiologist with extensive experienc chest work I should say that the majority of the 30% of "isolated, well-defined, spherical shadows" young Service patients with no symptoms were shad without the slightest clinical significance Patients h died after and during such investigations, and if had no symptoms before operation they have infrequently had them after it the mental disturb alone, can be serious Moreover, if the tuberculous is already healed its resection is unlikely to confe slightest benefit on the patient True, if left alo may break down, but, if that happens, a lesion w has healed once will probably do so again if the r of the patient is assisted Finally, have we any p that resection of a malignant lesion will cure the patie Are not the "successes" possibly due to errone interpretation of histological material? I have know patient diagnosed as having malignant disease live years after "mere biopsy" as the treatment, and have seen some spectacular radiographic lesions rem unchanged for as many and more years—until d followed attempts to remove them I have known resections for pneumonia

In the same issue of your journal Dr Bernard Le points out that medicine "has only slowly and pain won through to some sort of scientific basis" Is not fault in "some sort of scientific basis"? Dr Doml (Sept 5) and Dr Odlum (Sept 19) say that ther every need for reorientation in every branch of medi Recently a famous surgeon was quoted as saying

I advise the man who smokes heavily, especially if h over 40, to have a chest X ray every six months—or prefe

three months—so that the physician can find the
r if one develops while surgery can still cure it '

't from the truth that no-one has any right to claim
re would it not be wiser, if it can be proved that
ang is the certain cause, to prohibit smoking ? I
this though the radiologist, the physician, and the
eon would be deprived of work
is the theory of cellular pathology given us so much
that we need not consider ' reorientation ? It
s to me that the clinicians of the past learned more
bservation of the patient.

mingham JAMES F BRAILSFORD

JRGICAL TREATMENT OF VARICOSE VEINS

R,—Shortly after my arrival in Canada I first
hed, with horrified fascination, the removal in toto
varicose vein of the lower limb from saphenous
ing to internal malleolus Since then the horror
lessened and the fascination increased. I believe
to be a satisfactory operation, at its worst not less
tive than high ligation with or without retrograde
tion

Smithers
itish Columbia. KENNETH M. LEIGHTON

SUCCINYLCHOLINE CHLORIDE AND LIVER DAMAGE

R,—In his letter of July 11 Professor Macintosh
es that during his visit to India and Indonesia he
d that despite malnutrition and anæmia—and
umably ' liver damage —patients needed curare in
er doses than I had anticipated He also states that
ound that succinylcholine (Scoline ' Brevidil M)
aved in a similar manner
wo winters ago I spent the best part of three months
a lecture demonstration tour of Pakistan (East and
st) India, Ceylon Burma and Iraq and gained the
owing impressions :

avenous Anæsthetics

næsthetic drugs which are given intravenously and are
wn respiratory depressants had to be used with caution ;
rwise long periods of apnœa resulted. Many patients
ved marked muscular relaxation with what we in England
ld regard as modest doses of thiopentone ; for instance
H. Barat, anæsthetist at the Eden Hospital, Calcutta,
onstrated two anæsthetics for sterilisation of female
ents using thiopentone alone (i.e without additional
lation anæsthesia) in doses of 11 5 ml. and 14 ml. respec
ly By and large I gained the impression that the dosage
hiopentone required (Pentothal or Intraval) was
ut two thirds of that which I had been accustomed to
ng at home in England. Postoperative respiratory depres-
was most marked when pethidine had been used during
ations (perhaps because it is detoxicated almost entirely
the liver) and great vigilance had to be observed to
ent morphine being given *as a routine* after operations
ad of being *withheld until the patient complained of*

cular Relaxants

xcept in Iraq *d* tubocurarine and gallamine (Flaxedil)
required in about two-thirds to four fifths of the dose
was accustomed to use in England Scoline was not
onstrated as it was thought inadvisable to demonstrate
rug which at that time was still in the experimental

al and Extradural Anæsthesia

wing no doubt to the patients shortness of stature spinal
sthesia could often be induced with surprisingly small
s. For instance in Colombo I achieved spinal anæsthesia
panhysterectomy using only 8 ml. of 1 in 1500 solution
Nupercaine Admittedly the injection was given in the
ng up position, but the patient was placed on her back
oon as the injection had been finished and the puncture
swabbed with iodine Skin analgesia rose to the level
bout the eighth thoracic segment I feel quite sure that
anæsthetists would stake money on achieving analgesia
to this height with such small doses given to an average patient in the British Isles. Iraqis needed doses similar to our own particularly if they came from Kurdistan Owing to the low salt intake and the prevalence of vegetarianism (with the consequent consumption of second-class proteins) blood pressures in the Indian subcontinent are rather low and anæsthetists there are in the habit of giving spinal anæsthesia to any patient with a systolic blood pressure above 100 mm Hg When used for cæsarean section I found that spinal anæsthesia caused a similar drop in blood pressure to that in English patients ; it was, however sometimes difficult to restore the blood pressure to normal by the use of vasopressors. In one instance—a Chinese patient in Rangoon—prophylactic ephedrine and doses of methylamphetamine (Methedrine) during the operation failed to prevent a dangerous fall of blood pressure intravenous noradrenaline did however bring the blood pressure back to normal Using lignocaine (Xylocaine) extradural anæsthesia (sacral extradural and spinal extradural) required much the same dosage as is used for patients in Europe and the U S.A

Resuscitant Drugs

The effect of thiopentone and pethidine could be reversed quite readily by nikethamide (and a similar experimental drug issued privately by Imperial Chemicals [Pharmaceuticals] Ltd) in the usual doses. Neostigmine (with atropine) proved an adequate antidote to *d* tubocurarine and gallamine

It is of course difficult to know what Professor Macintosh had in mind when he used the words larger doses than I anticipated ; and it may be that he found as I did that the dose of *d* tubocurarine and gallamine ranged around 70% of that used in England Again when using several intravenous agents each of which is a central or peripheral respiratory depressant *it is often difficult to judge which of these drugs is* responsible for any excessive apnœa—i e Professor Macintosh may have used smaller doses of thiopentone than I was using and therefore required larger doses of the curare drug to secure quiet respiration and muscular relaxation I would be interested to know whether Professor Macintosh agrees with me that intravenous anæsthesia must only be administered to Asian patients in cautious doses.

King s College Hospital
London S.E.5 A H GALLEY

JUVENILE DELINQUENCY IN NORTH AMERICA

SIR,—In your article last week on this subject you state that it is rare in this country for a juvenile case to be heard in a criminal court What I assume you mean is that it is rare for a juvenile case to be heard in an adult court since all our juvenile courts are in fact criminal courts.

In this country the age of criminal responsibility is fixed at 8 years, which is much less than that fixed by any other country outside the British Commonwealth On the Continent it is generally 13 or 14 Children under that age some of whom would here be regarded as law breakers are dealt with by a child welfare organisation and not by any judicial process.

Our exceptionally low age of criminal responsibility is apt to strike foreign observers as both absurd and shocking and there are very real practical drawbacks to it Sometimes a child may appear before a juvenile court for whom some special treatment is clearly necessary but the magistrates may find their hands tied either because the evidence is not sufficient to prove the particular offence or because the police charge is not exactly in accordance with the facts Whatever steps they might like to take for the child s welfare they have no option but to dismiss the case

Another drawback of the status of our juvenile courts is that it leads to a hard and fast division between the treatment of the child labelled delinquent and the child labelled maladjusted, though as a matter of common sense such a division is meaningless So many maladjusted children are delinquent and so many delinquent children are maladjusted In a school where the staff is alive to the problems of the maladjusted, a child may be recognised as such at an early stage, and sent to a special school under the educational authorities Elsewhere a child of much the same type will be left to carry on until he finds himself in a juvenile court when he will be dealt with by the Home Office machinery, being either put on probation or sent to an approved school One cannot hope to get the most suitable treatment for the individual when it is so often a matter of chance which of two entirely different systems the child comes under

If we had welfare organisations on the Continental lines instead of criminal courts for children of school age, any child needing special treatment could be dealt with according to his needs Results would not be influenced by a rigid and artificial distinction

Howard League for Penal Reform,
Parliament Mansions,
Abbey Orchard Street,
London, S W 1

W A ELKIN
Hon librarian

LEGAL RESPONSIBILITY IN BLOOD-TRANSFUSION

SIR,—May I have the opportunity, perhaps, of allaying the fears expressed by Dr Leyton in his letter last week

I think I am correct in saying that the allergic manifestations of migraine are rather unlike those of the allergic conditions mentioned in my paper, in that it can only very rarely, if ever, be treated on allergic grounds, and secondly, if there is a sensitivity basis present, skin tests are never positive—i e , indicating that there are no circulating non-precipitating antibodies that can be demonstrated

Furthermore, recent work[1] shows that, genetically, there does not seem to be any evidence that migraine can be included among those allergic conditions which are considered unsuitable in a donor The possibility, however, of mendelian characteristics being transmitted by transfusion, an idea regretfully abandoned in the 17th century, reopens a vista of limitless extent

Where cases of the passive transfer of sensitivity from donor to recipient have occurred, the sensitisation is not of long duration, and, in fact, the chief problem in transfusion work is to avoid producing reactions in donors who have "reagins" in their plasma

Finally, I should be most grateful to Dr Leyton if he could produce any evidence, published or personal, that migraine is transmitted by transfusion

North London Blood Transfusion Centre,
Deansbrook Road
Edgware Middlesex.

J D JAMES
Director

CIRCUMCISION

SIR,—May I add a few remarks to those of "Sir Daniel Whiddon"? First of all some historical notes

According to the Bible, circumcision symbolised God's covenant with the people of Abraham—i e , all those belonging to the House of Abraham, including those of non Jewish origin (And ye shall circumcise the flesh of your foreskin and he that is eight days old shall be circumcised among you, every man child in your generations, he that is borne in the house, or bought with money of any stranger, which is not thy seed') This latter circumstance supports the hypothesis that circumcision was only a form of tribal marking, enabling the nomadic Jews to produce a secret sign of the fact of belonging to one tribe All other explanations of the purposive character of circumcision are of modern origin

At the time of the ancient Jews, circumcision was not practised by the Semitic tribes who surrounded them This transpires from the Bible in connection with the amorous adventure of Shehem, who wished to marry Dinah, Jacob's daughter, and was given permission on condition that every male of you be circumcised.

Apart from Jews, only Mohammedans practise circum (The term Mohammedan is not synonymous with Arab the Koran we find no references to circumcision on Hadish, the explanatory text of the Koran, mentions According to the latter Mohammed declared *hoft* (cir cision) to be compulsory on all his followers. Why the made compulsory ? No one knows with any degree of cert Educated Mohammedans, like Jews, mention hygienic re However, it is more likely that Mohammed, who that he and his people were the descendants of Ishmael was one of the sons of Abraham and the Egyptian H intended to establish a closer relationship between h his people, and Abraham himself by affirming the circumcision Abraham, by the way, is one of the imposing figures in the Koran Even the great festiv Beyramm commemorates the sacrifice of Isaac.

Modern Mohammedans and modern Jews try to a modern justification for the practice of circumc But the prepuce is no hindrance to personal hygie a person wishes to wash properly , its removal ha increased resistance to venereal diseases , and cision does not reduce sexual desire

The statements of Sir Daniel Whiddon should ever, be amended in one or two particulars First, human prepuce is not only a protective covering for glans penis, but, by the secretion of its glands (sme it gives the glans a greasy surface which facilitate entry into the vagina Secondly, Sir Daniel says the prepuce unfolds as the penis advances through vagina , but actually a normal prepuce is unfolded, and the glans is uncovered, at the tim erection Thirdly, in asking "Is there such a th a baby with phimosis ?" he replies "I have neve one" But phimosis is not uncommon among ba though rarely sufficient to obstruct urination, male babies have to be examined after birth to see they have phimosis or the condition termed cellularis preputii ad glandem which can be relieved after birth, but not so easily later On the other phimosis, when it is present, can be relieved eas plastic surgery even without recourse to circumc and the advantage of such operations is that the survives to perform its physiological function Sir Daniel's opinion that circumcision is a practice, to be avoided wherever possible

European Hospital,
Alexandria, Egypt

D A K

Appointments

HOPKINS G B , M B Birm., B PHARM Lond asst cou
Bucks County Council
JONES, O G M R C S D C P asst. pathologist (
Caernarvon and Anglesey H M C

Manchester Regional Hospital Board

COSTELLO SHEILA, M B Manc D.A consultant anæ
Bolton and district hospital centre
EDGE J R., M D Leeds, M R.C P consultant chest phy
Barrow in Furness hospital centre
FLETCHER D E , M B Leeds F F.R , D.M R D consult
logist, Barrow in Furness hospitals
MAY, W R M B Lond M R.C.P , D C.H consultant
physician, Rochdale and district hospital centre.
WARD JAMES M B Lpool D C P asst. pathologist,
Furness hospital centre

South East Metropolitan Regional Hospital Board:

ANDERSON A W M D Lond consultant in chest
Hastings hospital group
BRAIN R H F , M B Birm., F R C S consultant
surgeon, Brighton and Lewes and Preston Hall
group
COPE D H P M B Lond F F A R C.S consultant anæst
Lewisham hospital group
HART, W S M B Madras, D A consultant anæsthetist, W
hospital group
HUGHES D R M B , B.SC Wales M.R C O G consultant obst
and gynæcologist, Woolwich hospital group
KING M B M D Lond asst. pathologist, Bromley, Orp
and Sevenoaks hospital group
MITCHELL, P H , M A , M B Camb , D P.M asst. psych
Oakwood hospital group
TRETHOWAN J D , M B Camb , F R.C S , D.L.O consultant
surgery, Seamen's hospital group
WHITE S E , M R.C.S D O.M.S ophthalmologist Berm
and Southwark hospital group

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[1] Schwartz M Heredity in Genetical Asthma *Acta allerg*, Kbh 1952 5, suppl 2

Obituary

CHARLES BERNARD GOULDEN

O.B.E., M.A., M.D., M.Chir. Camb., F.R.C.S.

r Goulden consulting ophthalmic surgeon to the don Hospital, consulting surgeon to the Royal don Ophthalmic (Moorfields) Hospital, and formerly sulting oculist to the Household of Queen Mary l at his home at Shepreth on Sept 20, at the age 4

e was the eldest son of the late H J Goulden of terbury, and he was educated at St. Edmund's lege and at Downing College Cambridge Later always spoke gratefully of his years at Downing till then, he said he had had no outside interests opt music At Cambridge his horizon enlarged, but still worked hard for his parents were not wealthy he knew that he had his own way to make He pleted his medical education at the Middlesex spital, where he held a Freeman scholarship and a pold Hudson exhibition He took his M.B. in 1904 his F.R.C.S. a few months later After holding a se-appointment at the Middlesex he went to Moor ds, and one of his senior colleagues recalled him as e of the best house-surgeons we ever had' But could not afford the unrewarding first years of con ant practice in London, and after a period as onstrator in anatomy at the University of Bristol finally settled at Oldham where he was appointed to staff of the Royal Infirmary

n 1916 he left Oldham to serve in France where he ame Sir William Lister's right-hand man at Boulogne er he was put in charge of an ophthalmic centre at nen. For his work there he was mentioned in des ches and appointed O.B.E. in 1919 On demobilisation was offered an appointment at the London Hospital his Metropolitan colleagues welcomed his return n afterwards he joined the staff of the Victoria spital for Children in Tite Street and the Queen xandra Hospital Millbank He was also appointed the staff at Moorfields, where he soon became dean the medical school At the London Hospital he also ed in the work of teaching and became lecturer in thalmology at the medical college In due course also examined for the M.S. Lond the F.R.C.S. and D.O.M.S., and later he served on the board of advanced dies of the University of London and on the com tee of applied optics of the Imperial College of Science a teacher he showed the same qualities which served so well as a surgeon—precision of thought decision appropriate action meticulous attention to detail where necessary ruthless determination In 1924 published his Moorfields lectures for the D.O.M.S. rse, under the title of *Refraction of the Eye* and it characteristic of Goulden that he succeeded in king the section on optics no less lucid and interesting n the more clinical parts. In 1924 and again in 3 he was chosen to give the Montgomery lectures the Royal College of Surgeons in Ireland.

When the second world war began in 1939 he found ple scope for his energies first of all in the day-to- clinical work at The London and Moorfields and n as adviser to the Ministry of Health on the ophthal side of the Emergency Medical Service. His owledge of the men available and his understanding the needs of the different areas made his service aluable The strain however was severe, since this rk entailed much travelling in London and the Home nties. He lived partly in London and partly at preth and he experienced the difficult times of aerial nbardment. He also undertook the supervision of much of the actual work in the F.M.S. hospital at odmayes, and for a man of any age this volume of rk was most exacting

With the close of the war he retired from his appoint- nts at the London Hospital and at Moorfields. He l in fact left the latter rather earlier but had returned fill the place of younger men serving with the Forces. t though Goulden retired from hospital he continued private practice and in the years 1944–46 he was president of the Ophthalmological Society of the United Kingdom He filled this office with great distinction and his presidential address on Purkinje was an indication of his great interest in history Most of his address dealt with Purkinje's *Commentary on the Physiological Examination of the Organ of Sight and Cutaneous System* Goulden said this book was written in ecclesiastical Latin difficult to translate, and one suspects that he studied it in the original

M. H. W. recalls how just before the late war Goulden bought a delightful little house at Shepreth near Cambridge and as time went on he spent more of his time there and less in London. It was a sad blow to his friends when they heard that he had undergone a severe operation, but those *who visited him afterwards in the London Hospital* were filled with admiration at the physical and moral courage which he showed. This misfortune hastened his retirement from active work, and he now lived entirely at Shepreth where he enjoyed the beautiful surroundings and the opportunity of frequent visits to Cambridge to his old college Downing and to the dinners of the Cambridge Medical Graduates Club He continued to come to London also till very recently but when I called on him early this year could not fail to see how frail he had become though still retaining all the keen intelligent interest in affairs which he had always shown.

All of his friends must feel deeply the passing of one whose influence on the ophthalmological world especially on the side of education, has been so considerable and whose charming and often amusing companionship was always so acceptable

In 1911 Mr Goulden married Miss Norah O'Brien There were no children of the marriage

JOHN FRANCIS CARTER BRAINE

M.D. Durh., F.R.C.S., F.F.R., D.P.H.

Mr Carter Braine, director of the radiotherapeutic department of Guy's Hospital and civil consultant in radiotherapy to the Royal Navy, died at his home in Speldhurst on Sept 20

He qualified from Guy's Hospital in 1910 and at once joined the R.A.M.C. to serve in France and later in East Africa. On his return to Guy's at the end of the war he was appointed demonstrator of anatomy and in 1922 he took the F.R.C.S. a distinction also held by his father and grandfather For some years he worked in the department of pathology under Prof Adrian Stokes, and while Griffiths demonstrator he submitted the thesis for the M.D. of Durham University for which he was awarded the gold medal He held the post of chief assistant in the old actinotherapy department at Guy's before he was appointed to the staff as surgeon to the radiotherapy department in 1935 He was also a member of the staffs of the West London Hospital and *the King Edward VII Hospital Windsor*

During the late war Carter Braine acted as adviser in radiotherapy to the group officer and his help was of inestimable value in the organisation of radiology in the Guy's sector When the war broke out all the radiotherapy beds at Guy's were closed and the equipment was moved from London. One unit was taken to Sherwood *Park, Tunbridge Wells, and there by arrangement with* the medical school he was able to continue his clinical work When the Guy's U.S.A. Hospital was opened at the Wilderness near Sevenoaks, in 1941, it proved possible with his help to create, in hutted accommodation a radiotherapy department which remained in use until the end of the war when it was transferred to Pembury Hospital. During the whole period Carter Braine never spared himself and he must have covered well over 100 000 miles travelling between Tunbridge Wells, Pembury the Wilderness and London driving himself in all weathers and in the blackout

He was a foundation member of the Society of Radiotherapists of Great Britain and Ireland and he was a member of the official British delegation to the fifth International Congress of Radiology in Chicago in 1937 He also acted as assistant treasurer and member of the board of management of the sixth International Congress of Radiology in London in 1950

Three of his colleagues have sent us this joint tribute

"The first deep X ray plant in England was installed at Guy's, and from these early days Carter Braine worked unceasingly to improve techniques and results Few could claim the wealth of experience which he possessed His clinical judgment, tempered by a profound understanding of the suffering and anxiety of his patients, was an inspiration and challenge to all who worked with him His constant enthusiasm and encouragement evoked a loyalty in his staff which can seldom have been matched To his great generosity many can testify, and he unhesitatingly used his own equipment to treat hospital patients if he felt it was to their advantage Not least among his many talents was an ability for organisation, which reached its zenith during the war years

"Though his professional life was extremely busy he had wide interests outside his work He dearly loved the country and this was reflected in the careful husbandry of his farm He was interested in art and architecture, as well as all things mechanical, and he delighted in visiting factories and research departments to see for himself how things were made He was a keen and competent photographer, an interest reflected in the excellent clinical photographs and lecture slides of his department

"Despite his vast experience, he was the most modest and unpretentious of men His capacity for work was prodigious and, being physically very robust, his endurance was astonishing He had a great sense of humour and a temperament that was singularly equable He delighted to entertain, and his remarkable memory served him well in argument and discussion To his patients he was indeed the beloved physician, whose sympathy and understanding never failed"

Mr Carter Braine is survived by his wife and one daughter

SANTO WAYBURN JEGER
M.R C.S , M P

Dr Jeger, who has for the last eight years been one of the medical Members of Parliament, died on Sept 24 at the age of 55

He spent his early life in Cardiff, where he was educated at elementary and secondary schools and at the University College of South Wales Having completed his medical training at the London Hospital in 1923, he settled in general practice in Shoreditch, where he soon proved himself an able and popular doctor The strain of continued overwork in this heavily bombed district during the late war, and his responsibilities in charge of a mobile ambulance unit, contributed to the coronary thrombosis from which he never completely recovered

[Elliott & Fry

His political career also started in Shoreditch, for he was elected to the borough council in 1925, became mayor in 1930, and in the following year began his 15-year membership of the London County Council About this time he took an important part in the early activities of the Socialist Medical Association, and during the Spanish civil war he twice went to Spain on behalf of the Spanish Medical Aid Committee

In 1945, he was elected Labour Member of Parliament for South-East St Pancras, and after the redistribution of parliamentary constituencies he sat for Holborn and St. Pancras South In 1946 he visited Austria as a member of a Parliamentary delegation

B S , one of his medical colleagues in the House of Commons, writes

"Jeger served his constituents in Parliament as only a practising doctor can He brought into the House an atmosphere of realism tempered by his ideals and based upon his [illegible] contacts with the needy and the sick His special interests lay in the pursuit of remedies for the soci physical ailments of humanity For this reason he ardent supporter of the National Health Service, and speeches in support of the principles of a free and hensive service were models of close reasoning and right to a degree He was bitterly opposed to the im of any charge for any part of the service, and never to make his opposition clear His work as a doctor him to agitate for improved standards of housing that the slum house was his personal enemy, for in every he did we sensed in him his rôle of the physician

"All of us valued his friendship and his mature He had great experience as an administrator before he Parliament and this, combined with his idealism, opinions added weight He loved peace and cruelty The views he held on foreign affairs were a ago thought to be to the Left of some of his colleagues, are now such as almost everyone accepts

"Many of us have cause to remember him with grat for even in the House he was always helpful to those fell sick and needed his help That he worked too and was indifferent to his own suffering, does not any doctor For the pain and distress of others he too sensitive

"I will miss mostly his exquisit sense of humo well burnished weapon which he could use against as easily as against an opponent He could have lived had he so wished, but he preferred to live his life in full"

His wife, who is a journalist, is a member of the L and of Holborn Borough Council, and his brother is M P for Goole

KENNETH EDWARD ECKENSTEIN
M B Lond.

Dr Eckenstein, consulting physician and patholo the French Hospital in London and a former pres the Chelsea Clinical Society, died on Aug 23

He was born in 1881 in Liverpool, where his Wilhelm Eckenstein held the appointment of S consul, and he was educated at Uppingham He qua from St Thomas's Hospital in 1906, taking his M.B. L the following year After holding resident app at St Thomas's, at The Hospital for Sick Chi Great Ormond Street, at the Chelsea Hospital for Wo and at the French Hospital in London he became assistant to Professor Sabrazès at the clinical of Bordeaux, and with his chief he described a method of diagnosing syphilis by complement-fix In 1910 he returned to London to take up the ment of pathologist to the National Hospital for Di of the Heart His years of practice in London interrupted only by his service during the 1914-1 as a medical officer with the French army, for whi later received the Croix de Guerre and was appo chevalier of the Order of the Crown of Belgium and officer of the Legion of Honour

Though he was himself British-born, Dr Ecken spoke French perfectly and he had many contacts the French-speaking communities of London. Bes his appointment at the French Hospital he was physician to the French Consulate, medical insp London French Catholic Schools, consul of Mona London, and a correspondent of the *Swiss Observer*

For over forty years he was closely associated with Chelsea Clinical Society, which he served as secr president, and treasurer, holding this last office till end of his life He rarely missed a meeting and his and lively conversation added greatly to the int the dinners which traditionally precede these me He leaves a widow and one daughter

NEST KAHAN
M B Lond., D P M., D C.H.

Mrs Kahan, registrar at the Horton Hospital, Ep died on Sept 16 at the age of 42 Her maiden name Thomas, and she qualified from the Royal Free Hosp in 1934, taking her M B Lond three years later most of the late war she held an appointment as phys at the E M S Southern Hospital, Dartford, Kent W she gave up that appointment in 1947 her interest to psychiatry, but in 1948 her career was for the time interrupted by ill health She was appointed n Hospital in 1940 and for the greater part of her l of service there she held the position of registrar btained the D.P.M in 1952.

H W writes: 'Dr Kahan was a shrewd and l clinician and her experience and special qualifi s were invaluable during the difficult period when n Hospital was reverting to its original psychiatric ion She will be long remembered for her happy onship with both staff and patients and for her ne attitude to their problems During the last two she was often in pain and her steadfastness go, and devotion to duty were the admiration of all shared her secret"

r husband is Dr Alexander Kahan, consultant cian to St James Hospital, Balham, and she s a son and a daughter

Diary of the Week

OCT 4 TO 10

day, 6th

UTE OF DERMATOLOGY St. John's Hospital, Lisle Street C 2
P.M. Dr C. O Carter Principles of Genetics.

esday, 7th

. SOCIETY OF MEDICINE, 1, Wimpole Street, W 1
P.M. *Section of History of Medicine* Colonel H R. Gilmore (Washington, D C.): Medical Aspects of the Assassination of Abraham Lincoln Dr Bernard Freedman Last Illness of Dr Edward Wilson of the Antarctic.
M. *Section of Surgery* Sir Heneage Ogilvie: Life s Like That. (Presidential address)
UTE OF DERMATOLOGY
P.M. Dr H Haber: Normal Histology of the Skin.
UTE OF NEUROLOGY the National Hospital Queen Square C.1
P.M. Sir Francis Walshe F.R.S. Principles of Clinical Neurology
NICS SOCIETY
P.M (Burlington House Piccadilly W 1) Mr James Shields, B.A. Personality Differences and Neurotic Traits in Normal Twin Schoolchildren
SHIRE SOCIETY OF ANÆSTHETISTS
M. (Leeds General Infirmary) Dr W D Wylie Obstetrical Anæsthesia with Particular Reference to Cases with Cardiac Disease.
NCHESTER MEDICAL SOCIETY
P.M. (University of Manchester) Prof. John Morley: A Surgical Retrospect. (Presidential address.)

sday, 8th

SH POSTGRADUATE MEDICAL FEDERATION
P.M (Senate House, University of London, Malet Street, W C.1) Sir Henry Dale O.M., F.R.S: Scientific Method in Medical Research
ON OF GENERAL PRACTITIONERS
P.M. (Society of Apothecaries, Black Friars Lane, E C.4) Dr Geoffrey Barber Entry into and Setting up in General Practice
ON HOSPITAL MEDICAL COLLEGE, Turner Street, E.1
P.M. Sir James Spence: Varieties of Clinical Experience. (Schorstein lecture.)
L SOCIETY OF MEDICINE
M *Section of Ophthalmology* Mr J P F Lloyd Dr S A. E Hakim Epidemic Glaucoma.
M. *Section of Neurology* Dr E A Carmichael Pattern of Autonomic Function. (Presidential address)
D ADLER MEDICAL SOCIETY
M. (11 Chandos Street W 1) Discussion between Psychiatrists and Physicians on Psychological Reactions to Physical Disease
RSITY OF ST ANDREWS
M (Medical School, Small's Wynd Dundee.) Sir Russell Brain, P.R.C.P Consciousness and Unconsciousness.

ay, 9th

TUTE OF DERMATOLOGY
P.M Dr O L. S. Scott Developmental Abnormalities.

rday, 10th

I EAST METROPOLITAN REGIONAL TUBERCULOSIS SOCIETY
A.M (Grove Park Hospital Marvels Lane Lee, S E 12) Sir Geoffrey Todd, Dr James Maxwell Major Thomas C. Wright, U.S.A.F Mr F Ronald Edwards Brains Trust.

Births, Marriages, and Deaths

BIRTHS

EL.—On Sept 19 at Johannesburg South Africa, to Vera wife of Dr Eric Samuel—a daughter

DEATHS

ERMANN.—On Sept. 29 at Nottingham Ernst Zuckermann M.D Breslau L.R.C.P E.

Notes and News

INQUIRY INTO HEALTH VISITING

THE Ministers of Health and Education and the Secretary of State for Scotland have appointed a working party to advise on the proper field of work and the recruitment and training of health visitors in the National Health Service and School Health Service The chairman of the working party will be Sir Wilson Jameson F.R.C.P and its members are Dr A. Beauchamp (Birmingham) Alderman Mrs K. Chambers, O.B.E., LL.D J P (Bradford) Miss E G Himsworth R.G.N., S C.M (nursing supervisor for Midlothian and Peebles), Miss E. Stephenson, S.R.N S C.M. (chief nursing officer Newcastle upon Tyne) and Dr J F Warin (medical officer of health, Oxford) The working party will be advised by a steering committee also under the chairmanship of Sir Wilson Jameson on which the Government Departments concerned will be represented. This will have the expert advice on social workers and their training of Miss Eileen Younghusband, M.B.E., J.P., and Prof R. M Titmuss

The inquiry work on which will start this month, is expected to deal with the general position of the health visitor in the light of experience now gained—including for example, ways in which she might coöperate with the family doctor and the hospitals—but not with services with which the appointing Ministers are not directly concerned The joint secretaries to the inquiry are Mr R Pronger and Miss M H. Cook, S.R.N (Ministry of Health Chesham House, Regent Street London W 1)

TREASURES OF ORTHOPÆDICS

BEFORE concluding his term of office as president of the British Orthopædic Association, Sir REGINALD WATSON JONES with Lady Watson-Jones, gave a dinner at the Royal College of Surgeons on Sept. 25 when the guests included former presidents of the association and members of the executive. One of his aims as president he said had been to strengthen the younger generation s appreciation of what had been done by their forerunners and he had been disturbed at the thought of many of the historic treasures of orthopædics up and down the country being irretrievably lost With the help of Mrs. Hilda Watson and Lady Probyn-Jones (daughter and daughter in law of Sir Robert Jones) and others, he had in the past twelve months formed the nucleus of a national collection which would be housed for the association, at the Royal College of Surgeons. Local collections—at Liverpool and Oxford for example—should be maintained and extended; and to correlate all these possessions a new office had been created—that of keeper of the archives of the British Orthopædic Association (Robyn Jones doesn t know it yet but he is the keeper of the archives ")

Prof BRYAN MCFARLAND president-elect who presented a chisel used by Robert Jones at his last public operation said that such things were symbols evoking memories. From tradition springs the desire to emulate and if possible surpass the achievement of our predecessors, to maintain their high principles and to hold the ground they gained. Hillary and Tensing had climbed Everest on the shoulders of their fellows, and these on the shoulders of previous expeditions. Such reflections inspired collective pride but personal humility —a firm basis from which to hand on the treasures of the past

Sir THOMAS FAIRBANK recalled a day at Liverpool some 27 years ago when he assisted Robert Jones in conducting the second examination for the M.CH. ORTH and two of the four candidates were R Watson Jones and B L McFarland. He proposed the toast of Two Historic Treasures Happily Still with Us—the president and president elect Mr WILLIAM GISSANE, as a Birmingham surgeon spoke on behalf of what he called the dominions and colonies of orthopædics

The chief guest, Lady Probyn-Jones presented an embroidered smoking-cap belonging to Hugh Owen Thomas and Mrs. Watson had sent a portrait of her father by Copnall. Other exhibits included the signet ring and piccolo of H O Thomas his annotated interleaved copy of the 1st edition of a volume of contributions to medicine and surgery and the annotated letters (some in Welsh) of his great grandfather Evan Thomas which (said the President) give a vivid idea of the atmosphere of orthopædic surgery at that period. Among MSS. were letters on the foundation of the British Orthopædic Association, and among drawings some early etchings by Sir Thomas Fairbank.

From the College of Surgeons library and museum. Mr W R. Le Fanu and Mr W E Thompson showed books, specimens and instruments. The specimens included a series by Sir William Macewen illustrating the growth of bone and another on the transplantation of bone illustrating the essay with which E. W Hey-Groves won the Jacksonian prize in 1916

DANGER FROM THE FIRE

WINTER brings danger of death by burning, especially to children and old people Dr Leonard Colebrook, F R S, writes to remind us that the peak period for serious accidents is from November to April Since Oct 1 it has been an offence for any person to sell or hire an electric or gas-fire, or an oil burning space heater, which is not fitted with a guard conforming to prescribed safety regulations, but the Act does not apply to fires already installed in people's houses, and as Dr Colebrook points out, there are about 4½ million of these now in use, and about 12 million open solid fuel fires Many—perhaps most—of these are not fitted with an adequate dress guard A similar reminder from the London County Council says that every effort is being made—by posters, pamphlets, and working models, and through the teaching of health visitors—to warn mothers of young children of the risks they run by not providing guards There are many new designs of guards at reasonable cost, and these are stocked by the large stores

The London County Council, in a warning to citizens
bout the new law, points out that its public control com
ittee now has the unenviable duty of deciding whether
not to prosecute parents or others in charge of children
der 12 who have suffered serious or fatal accidents from any
pe of unguarded fire—not merely from coal fires, as used
be the case

'he commonest materials associated with burning accidents are cotton and artificial silk, both because they are ignited by short contact with a moderate heat, and because they propagate flames rapidly They are the materials most commonly worn by women and children, and at present there is no completely satisfactory way of making them permanently non flammable Dr Colebrook hopes, however, that before very long it will be possible to make them *much less* flammable, so that if they catch fire they will not cause any extensive burn They would inevitably be a little more costly Up to the present there has been little demand for them, so manufacturers have been reluctant to put them on the market Housewives should be encouraged to ask for them in order to hasten the supply

FRENCH WORK ON THE HEART AND BLOOD-VESSELS

WITH so much to read and so little time for reading, clinicians and laboratory workers alike must pick and choose among the myriad articles poured out yearly by the scientific world, and what more natural than to choose first among those in their native tongues? It is only too easy to overlook or ignore work done in countries with other languages, and this is the cause of much unnecessary duplication of research The Cultural Division of the French Embassy in the United States is doing something towards overcoming this difficulty by publishing in English bibliographical digests of French medical and scientific articles The first of these digests[1] was published last December, for circulation in the U S A, and is available from the office of the Cultural Division of the Embassy[2] It summarises over 500 articles on the heart and blood vessels which appeared during 1945–51 Prof René Leriche contributes a valuable review of cardiovascular surgery in France today In a foreword Prof André Cournand professor of medicine in Columbia University who—like Professor Leriche—is a member of the advisory board for the series, expresses his hope that the booklet will encourage American surgeons to familiarise themselves with current French work Here we find it a little easier to keep in touch with our colleagues over the way, but the English are notoriously weak on languages and these useful summaries will be as welcome here as they are in America

University of St Andrews

Sir Russell Brain, P R C P, is to deliver the inaugural post graduate lecture of the next session of the medical school Dundee, on Thursday, Oct 8 He is to speak on Consciousness and Unconsciousness

Royal College of Obstetricians and Gynæcologists

Leverhulme research scholarships for 1954 have been awarded to Ian Donald Joseph Gardiner, and Matthew Lindsay Paterson The Blair Bell lectureships for 1954 have been awarded to Thomas Everard Christopher Barns and Ian Donald

Charing Cross Hospital

Admiral Sir Philip Vian will deliver the inaugural
of the medical school at 3 P M on Friday, Oct 9, a
Royal College of Physicians, Pall Mall East, S W 1

Wessex Rahere Club

A dinner of this club will be held at the Lansdown C
Hotel, Bath, on Saturday, Oct 24 Membership of th
is open to all Barts men practising in the West (
Further details may be had from Mr A. Daunt B
the hon secretary, 11, The Circus, Bath

American Society for the Study of Sterility

This society is offering an award of $1000 for an ess
infertility and sterility The closing date is March 1,
Further details may be had from Dr Herbert H. T
secretary of the society, 920, South 19th Street, B
Alabama

Professional Nurses and Midwives Conference

This annual conference, which is held under the a
of the *Nursing Mirror*, will take place at Seymou
London, W 1, from Oct 12 to 16 under the preside
Sir William Gilliatt Medical speakers will includ
Arnold Walker, Mr R C Brook, Mr A B Wallace,
Geoffrey Marshall, Dr E B Strauss, Mr Kenneth B
Prof A M Claye, Dr Kenneth Maclean, and Prof C H C

International Orthopædic Congress

The sixth Congress of the International Society of
pædic Surgery and Traumatology will be held at Berne
Aug 30 to Sept 3, 1954 Subjects chosen for discussion in
Treatment of Scoliosis, Orthopædic and Traum-
Problems in Gerontology, Physiological Backgr
Maximal Performances in Sport, Arthrosis of the Hip
articulatory Tuberculosis, Physiology and Pathol
Locomotion, and Surgery of the Hand Further par
may be had from the secretary general of the
M Jean Delchef, 34, rue Montoyer, Brussels, Belgium

Seminar on the United Nations Children's Fund

The World Federation of United Nations Associat
holding a seminar in Paris from Oct 19 to 25 on the w
UNICEF Dr Charles A. Egger, director of the regional
of UNICEF, will give the opening address The
open to doctors, nurses, medical students, auxiliary m
personnel, social welfare workers, and others interes
child welfare Further information may be had fro
World Federation of United Nations Associations, 19,
Kléber, Paris XVI

Royal Victoria Hospital, Belfast

This hospital held a jubilee week from Sept 20 to
celebrate its years of service On Sept 24, at the ceremo
naming one of the wards in appreciation of the services
honorary medical staff (1792–1948), Viscountess Brookeb
unveiled a tablet honouring those who "served the p
of Ulster by day and by night giving ungrudgingly
knowledge and their skill for no fee and reward apart
privilege of helping others"

During the week Lady Wakehurst opened the Herber
department of neurosurgery and neurology, the first s
neurological unit in the province Mr C A Calvert has
appointed director of neurosurgery and Dr R S A
director of the department of neurology The departm
two floored pavilion, includes an operating and dia
centre a 54 bedded unit, and 26 extra beds for the de
logical department It has cost £70,000 and has been
out of free funds

CORRIGENDUM *The Work of a Regional Hospital*—
article by Dr F Avery Jones (Sept 12, p 556) W
General Hospital was stated to have 110 beds. *In fa*
hospital has 127 beds, and it has recently taken
annexe with 35 beds for chronic sick.

Sir Rudolph Peters F R S has been awarded the degree
by the University of Cincinnati.

Prof Joseph Trueta has been appointed a chevalier of the L
of Honour in recognition of his treatment of French wound
Britain during the late war

Sir Andrew Davidson chief medical officer of the D
Health for Scotland in response to invitations from the S
General of the United States Public Health Service the
minister of health of Canada and the American Public
Association, is to visit the U.S.A. and Canada during N
and the early part of December

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[1] French Bibliographical Digest no 1M December 1952

[2] 972 Fifth Avenue New York City 21 N Y U S A

ERNUTRITION AND UNDERNUTRITION

II EFFECTS *

R. A. McCance
C B E., M A , M D., Ph.D Camb , F R C P F R.S
FESSOR OF EXPERIMENTAL MEDICINE IN THE UNIVERSITY OF CAMBRIDGE

m the Medical Research Council Department of Experimental Medicine, Cambridge

Clinical and General

THE first quantitative way of studying the effects of ernutrition and undernutrition was to follow the ight of the body and it has remained the standard one ere is a wide range of normality in the body weight, wever and it is impossible at present to say where the al weight for height begins and ends. Studies of the nposition of the body (see later) have shown that it l not be the same for all individuals and that it should bably vary with activity age, and sex In a popula n which is enjoying economic prosperity more people overweight than underweight This is due to the position of fat in the subcutaneous tissues omentum nd the kidneys, and to some extent round the heart the distribution again varies with age and sex dwards 1950) In man the lean parts of the body do t account for much of the 'middle-aged spread,' but heart hypertrophies if the blood pressure rises, as it ds to do in obese people and hypertrophy of the liver d alimentary organs has been described in rats which eating enormous quantities of food. The ovaries of se animals decrease in weight (Brobeck et al. 1942– a) There is an enlargement of the kidneys and supra nals (Kennedy 1951)

The loss of weight which follows undernutrition has en investigated on man and animals. It was established Chossat (1843a and b) and has been confirmed many nes since, that the loss of weight—like the gain of ight which has just been described—is a composite ocess (Morgulis 1923) It may consist only in a loss of (see later) but in starvation and also in general under trition the weights of the organs fall—not all however the same extent. The brain bones, and kidneys lose ry little if any weight, whereas the muscles lose a great al, and so do the heart and the alimentary organs wards the close of the last century the loss of weight of e liver pancreas, and similar organs was shown histo gically to be due largely if not entirely to a decrease the size of the cell (Loukianow 1897 1898 1899) M. Harrison has now made these findings more antitative by chemical methods and fig 1 shows some the results which she obtained when she was working th us (Harrison 1953a and b)

The clinical effects of prolonged overnutrition are too ll known to most doctors to require any description re. Some of them however will be mentioned later this lecture. They vary from flat-foot and arthritis to ofuse sweating on the slightest exertion.

The results of severe and lasting undernutrition are ry distressing and have probably not been seen in this untry by anyone practising medicine today Very dernourished people have a characteristic walk and sture With knees slightly bent the trunk and arms ouch forward and the head droops towards the chest lelweg Larsen et al. 1952) The internal body tem rature remains very near the normal but the distribu on of blood between the skin and the internal organs anges quite early in the process of emaciation (Howarth 51) and undernourished people always feel cold. This adds to their misery and they wrap themselves up in any clothes or blankets they can obtain They lose the ability to hold urine in the bladder without an urgent desire to pass it, and also tend to make very large amounts of urine particularly on lying down The two together prevent them getting any restful sleep and towards the end they begin to form thin watery stools and are unable to control their passage It is probable that this diarrhœa is accentuated by atrophy of the glands lining the bowel wall, coupled with the nature of the food which these people are generally forced to eat. There is no evidence that it is due to any specific infection The diarrhœa and polyuria are perhaps the most demoralising aspects of the terminal stages of famine The undernutrition in Germany in 1946–47 was never bad enough to provide clinical cases of diarrhœa but polyuria was usual This was partly due to the large amounts of soup which were consumed morning, noon, and night but the polyuria should be regarded as part of the redistribution and accumulation of extracellular fluid which begins quite early in the syndrome and may appear clinically as œdema (McCance 1951) Undernourished people, particularly if they are exposed to the weather tend to get a dry scaly skin and sometimes hyperkeratosis (Keys, Brozek et al. 1950 McCance and Barrett 1951) In most people the blood pressure falls; the level of serum proteins tends to do the same and there is usually a mild degree of anæmia Some of the more puzzling effects of undernutrition are the enlargements of the parotids and of the male breasts (McCance et al 1951 Helweg Larsen et al. 1952)

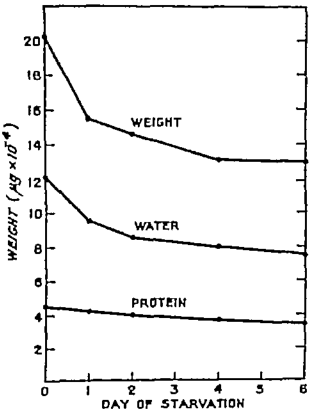

Fig 1—Effect of starvation on weight of liver cell of male rats and on weight of water and protein in it.

The Composition of the Body

The body may be regarded as being made up of the 'lean' portions and the fat Once the latter has been deposited, it may be considered as lying to some extent outside the active metabolic framework of the body The 'lean' can be further subdivided into the cell mass and the extracellular system and is very constant in composition during health. Until comparatively recent times chemical analysis of a body after death was the only way of getting at its composition and this method still remains the only one for certain purposes, and the most accurate one for most. In the 1930s however methods became available for estimating the volume of the extracellular parts of the body in living animals and in man. Knowledge thereupon increased and when it became possible to measure the total amount of water in the living body the physiologists were able to get some idea of the volume of the cell water by 'difference' The fat in the living animal and man was next assayed successfully by two independent methods One of these

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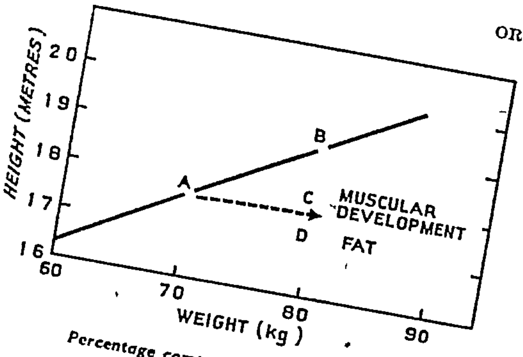
The second Humphry Davy Rolleston lecture for 1953 delivered before the Royal College of Physicians on May 7 Lecture I appeared in last week's issue.



Percentage composition of the body

	A	B	C	D
Cell mass	56 0	56·0	58 2	49·0
Extracellular fluid	21 0	21 0	21 7	18 4
Fat	16·0	16 0	14 0	26 5
Minerals	7 0	7 0	6 1	6 1

Fig 2—Effect of a gain in weight on the composition of the body

(Behnke 1942, 1945) depended upon the principle that fat and lean have different specific gravities By finding out the specific gravity of the body the percentage of fat in it could be calculated on the assumption that the lean part had a known and constant value The other depended upon finding out the total water in the body and hence the weight of "lean" in it The fat was derived from the difference between this and the weight of the body (Osserman et al 1950) A refinement of this method was worked out independently by McCance and Widdowson (1951) by which the weight of the cell mass was calculated from the cell water, and the weight of the extracellular system from its volume The fat was again derived from the difference between the sum of these figures together with the bony materials, and the body-weight The advantage of this method was that it could be applied to people with abnormal "leans"— with œdema for instance

TABLE I—PERCENTAGE OF FAT IN NORMAL MEN AND WOMEN

Men			Women		
Height (m)	Weight (kg)	% fat	Height (m)	Weight (kg)	% fat
1 65	62 8	18 1	1 60	63 0	16 0
1 67	56 8	17 9	1 62	63 2	19 8
1 74	81 2	22 4	1 64	74 0	28 5
1 80	62 1	10 3	1 64	75 5	21 5
1 80	72 2	15 2	1 68	55 2	12 0
1 81	56 3	7 2	1 75	79 2	21 1

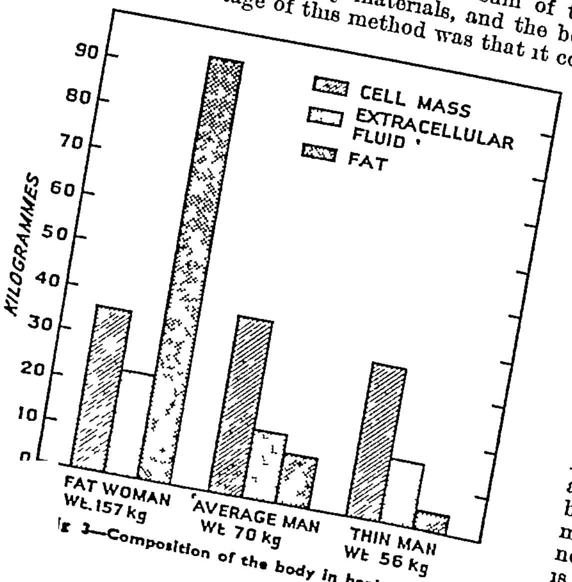


Fig 3—Composition of the body in health

Fig 2 shows the line relating normal weight and and the composition of the body of four ima young men, A, B, C, and D C differed from A muscular development, D only in the amount of his body Notice how three people of the same w can vary in composition, and that a light man may have exactly the same composition as a he man (B) if he is not so tall Table I shows the in the percentage of fat found by McCance and Widdo (1951) in a group of men and women, all of whom reg themselves as normal and were accepted as such for investigation The variations are large and shoul studied The lean parts of all these people were more constant in composition and always cont 70–72% of water

As people get older their weight tends to This is due to laying down fat, but another change takes place at the same time which masks the amounts actually being deposited This is the of cell mass due to reduced activity which gener accompanies advancing age (Brozek 1952) Welham Behnke (1942) have made a series of individual of the bodies of athletic young men, and compared with those of groups of naval men who were not athl When the sailors and the athletes were the same the former were found to contain much more fat and correspondingly less muscle (see fig 2) Brozek (1952) has made a study of active and sedentary middle-aged men and obtained a similar result

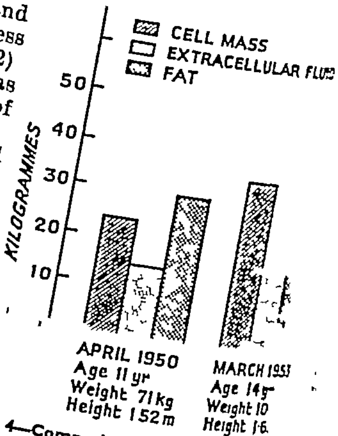
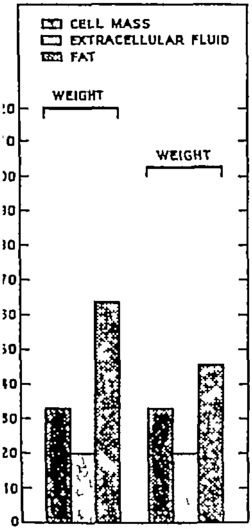


Fig 4—Composition of the body of a

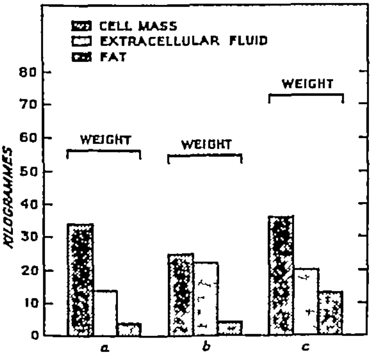
Fig 3 shows the composition of the body of a very fat woman and of that old friend the 70-kg man whom we have all known from our student days I have taken the liberty of adding myself as an example of a thin person The mous amounts of fat being carried about by Gross are a terrible warning to the overindulg Not that they are records by any means Lambert, whose height was 5 ft 11 in, weighed 73 when he died (aged 39) in 1809 (Gould and Pyle Encyclopædia Britannica 1910–11), I expect that 530 lb, or 240 kg, of this was fat Coe (1751–52) a grocer of height 5 ft 9 in who died at the age weighing 616 lb—probably 425 lb, or 192 kg, of it fat Women have been recorded up to 850 lb 1878, Correspondant, France 1890), which make Gross seem light, but even her burden weighed than the 70 kg man did, and still more than I do furthermore, Mrs Gross had no more cell mass th have with which to carry about all this weight wonder her complaint was breathlessness. There another rather interesting thing about her She little too much extracellular fluid in her "lean" (and Mach 1949) This may be regarded as the blood, lymph, and tissue fluids necessary for the nour ment of that great mass of fat Quantitative work no support to the views of those who believe that is due to a retention of water (Oertel 1891, von N 1910, Grafe 1920, Copeman 1950, Greene 1950, burger and Mathé 1952) ig 4 shows the progress of obesity in a boy aged 11 rs when first seen and aged 14 when next investigated added 18 cm to his height in this time and developed his muscular mass to some extent but more than half of his increase in weight was due to fat, and the proportions of his body changed for the worse



5—Composition of a fat woman (a) and e same woman after “ slimming (b)

If an obese person s weight is reduced by a diet containing enough protein to maintain the cell mass the evidence is that the loss of weight is entirely due to a loss of fat The N balance is not negative (Newburgh 1944) Fig 5 shows results which we have ourselves obtained

Fig 6 shows the composition of a very undernourished man He was a German, just back from a Russian labour camp I have again inserted myself for comparison, and 6 also shows the effect of two months ease and plenty the undernourished German He had very little fat his body when he first came back but so have I it is clear that a small amount of fat in the body is proof of undernutrition A rapid fall in the amount etter evidence, but the most characteristic feature real undernutrition is an increase in the amount of racellular fluid in the lean ' and a decrease in the mass This only begins to happen to any extent after siderable loss of weight, unless the protein intake is fficient to meet the body s requirements, when it' st begin to happen from the first



6—Composition of a thin man (a) an undernourished man (b) and the undernourished man after rehabilitation (c)

There is no difficulty about explaining most of these changes The deposition of fat is due to the food entering the system providing more energy than the activities of the body demand. The loss of fat and cell mass in undernutrition are equally simply explained They have been mobilised and metabolised to provide the energy and amino-acids for organs like the kidney, brain and heart which have maintained the essential services of the body The increase in extracellular fluid is probably due to a number of causes. Replacement is certainly one As the fat in the marrow is removed its place is taken by extracellular fluid A vacuum in the bones would be impossible, and extracellular fluid is the only material with which the spaces previously occupied by fat could be filled As undernutrition gets worse the large deposits of fat round the kidney and in other sites become spongy masses of connective tissue and extracellular fluid Similar changes take place in the subcutaneous tissues Another reason for the increase in extracellular fluid in the body is the change in the relationship of surface area to body weight Surface area decreases much less than the body weight and consequently the large amounts of extracellular fluid in the skin come to contribute more and more to the body weight There may be changes in the level of suprarenal activity, and many other suggestions have been made but they must all for the moment be regarded as non proven (McCance 1951)

With so much extracellular fluid in the body and the loss of coherence between the cells, it is curious that all undernourished people do not get great collections of extracellular fluid in the dependent parts Some do and hunger œdema has become one of the proof marks of advanced undernutrition ; but it is surprisingly uncommon People can die of chronic undernutrition without ever having had œdema Animals very rarely get it If it does appear in man its volume is usually only a small fraction of that of the surplus extracellular fluid which the sufferer is carrying, and its appearance should be regarded as an incident rather than a milestone in the march of the disease (Widdowson and McCance 1951),

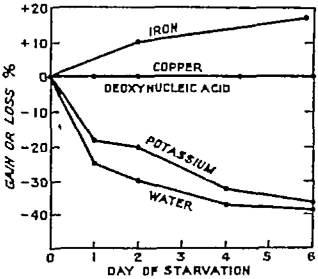


Fig 7—Percentage gains or losses of minerals from liver cell of male rats.

The changes which have been discussed are characteristic of the body as a whole but not necessarily of the organs or of the cells. Starvation for six days did not increase the percentage of extracellular fluid in the liver of rats, nor reduce the percentage of protein, although the weight of the organ fell and of the cells in it (Harrison 1953b) The loss of weight was largely due to the loss of protein and water in the proportions in which they were initially present in the cells (fig 1) but the percentage of fat actually rose in female cells Fig 7 shows other observations that have recently been made The cells lost no desoxynucleic acid or copper—both constituents of the nucleus—and consequently their percentage in the liver as a whole would have gone up The amount of iron in the liver cell may actually increase due to the deposition of iron which has become functionally redundant elsewhere in the body Water and potassium fell in equivalent amounts so that there was no osmotic or

TABLE II—PROTEIN KATABOLISM AND OXYGEN CONSUMPTION DURING STARVATION

—	Infants	Young men	Old men
B M R (cals /kg /24 hr)	50	26	21
Nitrogen katabolised (g /kg /24 hr)	0 075	0 17	0 12
Percentage of calories derived from protein	4	15–20	15–20

ionic disorganisation These findings bring to mind Gamble, Ross, and Tisdall's classical work in 1923, and help us to understand how surprisingly normal an undernourished person or animal may remain If undernutrition produced changes in the composition or in the osmotic pressure of the body fluids, as well as in their volume, its effects would be far more devastating than they are

Fragmentary as these observations are at present, they demonstrate the great risk of premature generalisations about the results of overnutrition and undernutrition Their effects must be expected to vary according to the system upon which attention is being directed Organs may not behave like the body as a whole, and the composition at the start must make a difference to the train of events later on Unlike the liver cells of the healthy adult female rat, for instance, which contain almost no fat, the liver of the newborn guineapig contains 12% of fat, and undernutrition may reduce this in a fortnight to 5% Age also must be expected to alter the effects of overnutrition and undernutrition We have recently been investigating a very striking instance of this (table II) Protein provides about 19% of the basal energy requirements of a healthy starving man, and he breaks down about 0 17% of his body nitrogen per kg of body weight per day This was well known, or at any rate the information necessary to establish the point was obtained many years ago We have recently found, however, that protein provides only about 4% of the basal energy requirements of a normal newborn baby, so that, in spite of his higher basal metabolic rate per kg of body-weight, he breaks down in starvation only 0 075 g of his body nitrogen per kg of body-weight per day (McCance and Strangeways 1954) We have no knowledge at present of how the protein is held in the tissues, but we may think of it tentatively as being due to the action of a growth hormone which continues even during starvation to direct the metabolic turnover of amino acids towards anabolism (Greenbaum 1953)

Growth and Longevity

There are often great differences between the sizes of two littermates One piglet, for example, may be three times the size of another, probably because of differences in the nutrition of the two fœtuses *in utero* The placing of a placenta may make all the difference between success and failure There is probably a limit to the amount of nutrients which a mother can pass to her young *in utero*, for twins are generally smaller than single babies (Blegen 1953), and this is true of animals also (Hammond 1952)

The weights of the infants born in an undernourished community appear to be slightly smaller than those born in the same community if it is in good nutritional shape (Smith 1947a and b, Keys, Brozek et al 1950, Dean 1951) These differences may seem small, but they may be made much larger in animals and can be magnified in man also if the tendency of overnourished and obese women to produce very large babies is taken into account (Jackson 1952) Hammond and his fellow workers (1952) have shown the importance of a high plane of nutrition during the last weeks of pregnancy in domestic animals if strong and fully developed offspring are to be expected at term The young of a mother on a low plane of nutrit re anatomically and physiologically immature, and, although they are the correct calendar age at they resemble the premature offspring of a moth high plane of nutrition In other words und has delayed the whole process of development wi otherwise interfering with it, so that the animal's logical age is younger than its calendar age would one to expect If the gestation period of the mother a low plane of nutrition could be artificially prol by progesterone for instance, the probability is would ultimately deliver themselves of young were some weeks or months older by calendar from conception date than their developmental (i.e., biological) age would suggest

Undernutrition also delays the growth of animals birth and may modify their form for any given calen age The farm animals have been studied more any others (Hammond 1952), but the same fact often been demonstrated in rats, and also that th animals have the capacity to make good this defi their biological development if they are given the ch It has also been shown, however, that protracted nutrition in rats not only greatly delays the rate of but also very materially prolongs the calendar life of animals (McCay et al 1939, McCay 1952) Senility takes them only when they are allowed to eat the and so complete their development and become It seems desirable that more of these experiments be done particularly on other animals which do not tinue like the rat to grow slowly throughout most of lives Only thus will it be possible to find out w the epiphyses in the long bones remain ununited enough to enable all such animals to attain a reason normal size Nutrition may not be the cause of difference (Ministry of Health 1953), but if the he attained by wealthy and slum populations are indication of what might be expected to happen in it would look as though the epiphyses would unite a perpetually undernourished youth could attain the stature to which he was heir The effect of reta growth of animals on their mental development offe wonderful field of investigation to anyone who acquire the necessary facilities

Part of our work in Germany in 1946 was to effects of a change of diet on a group of children who were known to have had a low calorie for some years These children were shorter and than English and American children of the same cale age Their "bone age" was also younger The of diet provided the children with unlimited cal largely in the form of bread It also provided calcium and vitamin D, although there is no evide that the children were in need of the vitamin A year of unlimited calories the children were nearly a and heavy as English and American children of calendar ages and their bone age had also increased nearly two years They were, like the rats, making for lost time, but by raising their rate of developm in this way the children's biological age was by nearly two years within the space of only one the calendar This may have been a nutritional but further reflection leads me to suggest that we have taken six to twelve months off those childr expectation of life by feeding them up in this way "T race is not" necessarily "to the swift nor the battl the strong but time and chance happeneth them all" (*Ecclesiastes*, chap 9, verse 11) We may shortening the lives of the generation now growing up this country by trying to make them grow faster school meals and school milk

Children who are generally overweight have been fo to be taller and to have an older bone age than th calendar age would lead one to expect (Bruch Le Marquand 1951) There is, therefore, some evid that the rate of growth can be forced by overfeed w this comes about is at present a matter of conjecture there are two possibilities Firstly if overnutrition ls initially to hypertrophy of the islets of Langerhans ch insulin may be available and liberated in the body ing the earlier years of a career of overnutrition—and re is evidence that insulin can act as a growth hormone st 1952) Secondly the more food eaten the more va is likely to be produced and swallowed and if inados (1951) is correct in finding that human saliva tains a growth promoting factor for the golden nster it may possibly contain one for man himself l perhaps be one of the factors which helps to keep rition and growth ' in step

)vernutrition and obesity certainly tend to shorten adult's life All are agreed about this life-assurance tistics show it (Newburgh 1944 Evans 1952) animal periments confirm it (McCay et al 1941, Kennedy il Hansson et al 1953) To some extent this mature demise may be attributed to purely mechani causes The rats for example get so fat that y become almost immobile. They are no longer e to clean themselves they drag themselves round ir cages and parts of the skin which are subjected to isual pressure or friction lose their fur and ulcerate e fat man is more likely to break his ankle or his iur if he slips off the kerb and he is always a worse ration risk than the thinner man in the next bed

)vernutrition however interferes with the expectation life in much more fundamental ways than these insson et al. 1953), and some instances of its effects st be considered There has been a controversy many years as *to its influence on the composition* the serum The level of cholesterol therein has n the focus of interest owing to its relation to erial degeneration from which the overnourished particularly liable to suffer (Gardner and Gains ough 1928 Okey and Stewart 1932–33 Steiner l Domanski 1941 Gertler Garn and Lerman 1950 rtler Garn and White 1950, Moses et al 1952) en et al (1952) found that a frugal vegetarian diet ded to give lower values in the serum even in young ilts, than a rich diet containing much meat, cheese l eggs, but the most important contributions to this ject in recent years seem to have been those of Keys l his fellow workers (Keys Mickelsen et al. 1950 ys et al. 1952) Keys (1952) pointed out that some ple and some families have naturally high serum olesterol and that they tend to get arteriosclerosis very ing He also showed that, in man putting up the lesterol intake at any age did not usually raise the um-cholesterol although it had some effect in old ple According to him the serum-cholesterol tends to rease with age, and this is due to the consumption not much of cholesterol as of fat In undernourished nmunities the serum cholesterol may even fall after age of 35 and if the intake of fat is kept very low it y not continue to rise after this age even if the nutri n is adequate We can confirm these findings about um levels in undernutrition from a limited series of n who were investigated in Germany in 1946 (fig 8) erlock and Walshe 1951)

A high blood pressure is one of the results of over ing although there is always some uncertainty about measurement in very fat people The change seems precede arterial degeneration and may perhaps be a se of it. At all events hypertension has been shown be associated with obesity in quite young people (Odell l Mengert 1945) and the fat boy of 14 to whom refer e has already been made has a blood pressure of)/80

)vernutrition certainly predisposes to diabetes. This is true of mice (Mayer et al. 1952) as of men (Evans 12) Are we to assume that this is due to arterial eneration of the vessels supplying the islets? Probably not, because in the mice the islets are hypertrophied when the animals get diabetes and moreover undernutrition in any community decreases the incidence and mortality from diabetes so that the plane of nutrition itself seems to be the important variable. It seems more reasonable to regard the diabetes of overnutrition as a failure of the islet tissue to keep pace with the metabolic demands made upon it A similar reason may underlie the other pathological lesions which have been described in the kidneys and other organs of obese animals (Brobeck et al. 1942–43a, Brobeck 1946 Bleisch et al 1952) In other words these lesions are not just the secondary effects of a rise in the serum-cholesterol and arteriosclerosis but are really specific signs of premature old age and the converse of the prolongation of youth conferred by undernutrition The latter is a much more stimulating thought Underfeeding has been shown to prolong the life of a protozoon, *Tokophrya infusionum* (Rudzinska 1951) Forcing the metabolic pace may well turn out to be an ageing factor in cells in many parts of the body of higher animals, and it is certainly possible that the easiest way to add five years to man's expectation of life would be to prolong his years of growth on the calendar by controlled undernutrition and to maintain him on a low plane of nutrition for the rest of his life The infectious diseases like tuberculosis might cause trouble but if the brave new world of the future is ever enticing enough to make a man wish to pay this price for another five years in it, such things may have ceased to trouble us For the dyet of youth is not convenient for old age nor contrariwise (Cogan 1588)

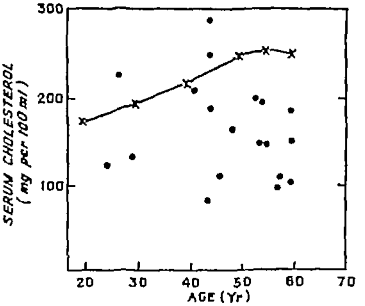


Fig 8—Cholesterol in serum of American citizens and undernourished German men: X——X, average for 1500 men in Minnesota; ● individual undernourished men in Germany in 1946.

Psychological Effects

Restlessness, movement and overactivity seem to be very fundamental aspects of mild undernutrition They are displayed by animals as low in the scale of evolution as hydra which is only 2 cells in thickness and possesses a most primitive nervous system (Buchsbaum 1953) as well as by mammals like rats which when they are underfed behave in rather a characteristic way They are always on the move they leap up on the side of the cage *whenever they are approached* and when they are given food they do not eat it quietly in the normal fashion but carry it about and try to make little piles of it in the corners. These their fellows at once steal and place elsewhere—and so the act goes on Rats deprived of all food behave rather differently in our experience and tend to lie huddled together after a day or two without much movement A considerable amount of work has been done on the increased movement of hungry rats (see Keys, Brozek et al 1950) and much more might profitably be done on the basic effects of overnutrition and undernutrition on animal behaviour So far as man is concerned a good state of nutrition is essential for mental contentment, and the converse would appear also to be true, for psychological trauma can impede growth (Widdowson 1951)

A disinclination for physical exertion often makes fat people appear placid, and they may be—in fact this may be one of the reasons why they are fat But some of the men who have made their mark on history have been distinctly stout—William the Conqueror, for instance, and Sir Winston Churchill When Julius Cæsar wished to have men about him that were fat, he really meant, I think, well nourished men, and fatness was his proof of this

The psychological effects of undernutrition have a literature which goes back to the dawn of history (Keys, Brozek et al 1950, McCance 1951, Helweg Larsen et al 1952) No summary of it can possibly do justice to the force and pathos of the originals Famine in some shape or form has been the lot of prisoners, castaways, explorers, the populations of cities, and even of whole countries, and, although the writers have mostly been sufferers as well, and consequently liable to subjective bias, the accounts they have given leave no doubt about the effects of famine on behaviour

As food gets short, people begin to get very careful about wasting it Later everything that can be eaten is diligently sought, and leaves, grass, and even earth may be taken in the hope of deriving some help from them (McCance 1951) Where hunger and satiety are fellow citizens, the rubbish-bins of the rich are scavenged for everything edible in them by the starving poor As the famine gets worse, food begins to occupy more and more of people's thoughts, other interests lapse and after a time it becomes the only topic of conversation and the cause of ceaseless activity Loyalties change as the organisation of society breaks down At first any food obtained will be shared with the family or group which has a common table This was the position in Wuppertal when we were there in 1946–47 When a small present of food was taken to someone in a German family it was obvious that everyone in the household would have the chance of sharing it, but the parcel was at once concealed if the doorbell rang for another visitor—all very reminiscent of the undernourished rats When famine gets very bad it tends to become a matter of every man for himself The behaviour of the " population " as a whole depends upon its morale If this is good—and it has been very good in many of the picked parties of explorers who have run short of food (Shackleton 1909, and see Keys Brozek et al 1950)—this last stage may be postponed almost indefinitely It probably developed most rapidly and was to be seen at its worst in the concentration camps, where group loyalties were almost non existent " Fights and flogging practically always attended the distribution of food, calling to mind the feeding of animals at the zoo " (Helweg-Larsen et al 1952) Whatever the morale, standards of behaviour always tend to fall with the supplies of food Black-marketeering, thieving, plunder, and even murder become commonplace events and no power on earth can prevent them

In the last stages people may become completely apathetic to all that goes on around them They lose all their self-esteem, their interest in their neighbours, male or female, and even in the struggle for food When this happens the end is not very far away

Closing Reflections

Hitherto research on nutrition has been directed largely by circumstances or economic reasons Wars have led to widespread undernutrition, prosperity has filled the clinics with preventable obesity—and consequently both have been studied Animal husbandmen have bred and fed their animals for rapid maturity and marketable [illegible] and political husbandmen have come near to doing the same for children Curiously little thought has been devoted to a study of the plane of nutrition for the different years of endeavour

Why such a plane should be desirable and achieve it have been still less considered Yet, by the figures for infantile mortality, the child of size at the time of delivery stands a better survival than an underdeveloped one or one which grown too great in utero The reasons are often enough, but how to produce the happy mean matter It would, however, be a minor preventive medicine if all babies could be delivery weighing between 6½ and 7½ lb We define the desirable levels of nutrition later in life, yet how they can be achieved They have not studied realistically Haldane (1940) once wrote essay " on being the right size " One day someone write a book " on being in the right plane of There is one, that is certain, for every age, but necessary to drink 500 ml of milk a day throughout or to eat 50 g of animal protein in order to Some politicians are sure it is, but I am not hope not, for I see no hope of providing the millions of this world with either of these good

I have a feeling that we should think of how to that happy mean in matters of nutrition which enable us to reduce infantile mortality and to the vigour of life from being weakened by the onset of old age *μηδὲν ἄγαν* may well turn out the legend for one of the signposts on the road to health

These lectures have been prepared jointly with Dr Widdowson I have had the privilege of delivering if they have any merit, half of it is due to her

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TRANSFUSION BY THE INTRA-ARTERIAL ROUTE

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THIS paper is based on one read in 1951 before the Association of Surgeons of Great Britain and Ireland its purpose is to indicate the benefits, in certain circumstances, of retrograde intra arterial transfusion and to discuss the possible dangers if solutions other than blood are used

The history of intra-arterial transfusion dates back to the beginning of this century Nearly fifty years ago Crile and Dolley (1906) showed that retrograde arterial perfusion with Ringer's solution to which adrenaline and hirudin had been added would consistently restart a heart stopped by an overdose of chloroform or ether This response was elicited up to 5 minutes after cardiac arrest and despite the failure of cardiac massage

This fact supported the findings of Sollman (cited by Crile and Dolley 1906) who postulated that the initiation of cardiac action depended on raising the coronary perfusion pressure to 30 or 40 mm. Hg and was not influenced by the quality of the perfusing fluid indeed Sollman restarted the heart in physiological preparations by perfusing the coronary arteries with mercury Once cardiac action had been initiated however the quality of the perfusant was important if the heart beat was to continue

Little attention seems to have been paid to these findings, for few references to arterial perfusion were published before Kemp (1933) suggested that retrograde arterial perfusion with physiological saline solution should be tried in man as a heroic measure to restart the heart after cardiac arrest during an operation

This method of treatment again lapsed into obscurity until Birillo (1939) and Negovsky (1945) claimed considerable success with it Since then several short papers have appeared, mainly in America each claiming that retrograde arterial perfusion has advantages over the normal intravenous route but almost all emphasising the danger that local gangrene might follow its use (Kohlstaedt and Page 1943 Porter et al 1948 Page 1947 Haxton 1952 Devitt and Widgerow 1951 Bayles 1951 Bingham 1952)

While trying to produce by bleeding a controllable level of circulatory depression in dogs, Kohlstaedt and Page (1943) found that the resulting hypotension could be more satisfactorily treated by intra arterial than by intravenous replacement of blood.

Clinical Evidence

Experience in the departments of anæsthetics and surgical neurology of Edinburgh University concerns cases in which retrograde intra arterial injection is used to replace blood purposely withdrawn in the technique of preoperative exsanguination or lost accidentally when large vessels are torn during the removal of a vascular tumour

For the past four years preoperative bleeding of the patient has been used as an aid in certain intracranial operations Following premedication with Nembutal gr 3 and atropine gr $^1/_{100}$ an hour before the operation anæsthesia was induced with thiopentone 0·5 g., and the larynx was intubated under direct vision anæsthesia being maintained with nitrous oxide and oxygen

After infiltration of the surrounding tissues with 2% procaine solution the radial artery was exposed through a small transverse incision over the artery about 2 in proximal to the radial styloid process. The artery was tied a small incision made in the vessel proximal to this ligature and a cannula inserted which was connected to a damped aneroid manometer and the blood-taking and transfusion set and was kept free from clots with intermittent injections of 1% sodium citrate solution in saline solution

When the operation was about to start, blood was rapidly withdrawn into a bottle containing the appropriate amount of sodium citrate until the desired degree of reactionary vasoconstriction was produced This was usually achieved by the withdrawal of 500–1000 ml, the systolic blood-pressure falling to about 80–90 mm Hg and the pulse rate rising to not more than 120 The blood pressure was maintained at the desired level by the addition or subtraction of such volumes of blood as were necessary The blood-pressure was recorded directly from the manometer connected to the radial artery as well as by auscultation over the brachial artery of the other arm

During the infusion of blood there was no recon
change in blood-pressure except for a very transient
of about 5 mm Hg at the start and a momentary c
parable fall on its completion Thereafter the bl
pressure remained constant for 2–5 minutes and t
rose to a new level over the next 10 minutes

Even after prolonged hypotension, lasting up t
hours or more, the addition of a relatively small vol
of blood intra-arterially was often sufficient to raise
systolic pressure from 70 to 80 mm Hg

In an attempt to compare the responses to intra
and intra arterial injection, transfusions of 100
blood were given at the rate of 8 ml a second. In
case the intravenous injection preceded the arterial
by half an hour, during which the patients' circu
responses were recorded A similar observation pe
followed arterial transfusion

RESPONSES TO INTRA-ARTERIAL BLOOD-TRANSFUSION

Case no	Time	Blood pressure (mm. Hg)	Blood flow below knee (%)	Blood flow with foot occluded (%)	Pulse rate	Change in blood volume (ml.)
1	10 00 A.M.	120/80	100	100		
	10 10	110/80	80	66		−500
	10 40	90/80	80	50		
	11 00	90/70	100	85		
	11 50	86/70	70	50		Artefact
	12 09 P.M.	90/70	60	50		
	12 10	90/70	60	50		+100 ml I.V (8 ml. per sec)
	12 15 "	90/70	60	50		
	12 30	85/60	60			
	12 49	75/60	40	33		
	12 50 "	75/60	50	40		+100 ml I.A (8 ml per sec)
	12 52	80/60	50	45		
	12 55	90/60	60	50		
	2 00	100/60	110	100		+400 ml I.A
2	10 30 A.M.	110/80	100	100		
	10 40 "	110/85	120	110		−500 ml
	10 50	90/80	66	50		
	11 00 "	90/80	58	45		−250 ml
	11 30	90/75	58	45		
	12 00 noon	90/75	66	50		+100 ml. I.V (8 ml per sec)
	12 30 P.M.	90/75	66	50		
	12 32	95/80	75	70		+100 ml I.A. (8 ml per sec)
	12 33	100/80	90	90		
	1 00	100/80	80	75		
	1 30 "	110/70	110	120		+650 ml I.A
	10 15 A.M.	100/80	100			
	10 20	75/70				−750 ml
	10 30 "	80/70	64			
	Intermediate results altered by hypothalamic stimulation					
	12 30 P.M.	90/60	40			
	1 00	90/60	54			
	1 08 "	100/60	20			
	1 09					Hypothalamic stimulation +50 ml I.A
	1 10	100/60	46			
	1 20	90/60	33			
	1 40	110/60	73			
4	11 30 A.M.	110/70	100			+700 ml I.A
	11 35	95/80	90			
	11 45	110/90	70			−500 ml
	12 00 noon	110/95	50			
	12 30 P.M.	105/90	30			−250 ml
	12 45	90/80	20			
	12 50	90/80	110			
	12 51	90/80	20			Measured during transfusion of +200 ml I.A (8 ml per sec)
	12 53 P.M.	90/80	30			
		Cuff of recording chamber punctured				
5	1 00	110/70	100			
	1 30 "	100/70	113			−750 ml.
	1 50 "	100/50	73			
	2 05 "	100/60	65			
	2 10	100/60	40			−750 ml.
	2 20	100/55	20			
	2 25	100/50	40			+60 ml. I.A per sec.)
	2 27 "	100/50	46			
	2 30 "	125/60	54			
	2 35	130/70	54			
	2 45 "	130/60	66			
	3 00 "	130/60	66			
6	12 00 noon	100/70	100			
	12 10 P.M.	100/70	80			−500 ml.
	12 15 "	90/70	40			−250 ml
	12 20	80/65	20			−250 ml.
	2 00	75/60	20			
	2 02 "	75/60	60			
	2 04	75/60	70			Measured transfusio +100 ml (8 ml per
	2 05	90/60	100			
	2 10	80/60	180			
	2 30	85/60	120			
	3 00	80/60	50			
	4 00 "	80/60	40			
	5 00	90/60	20			
	5 30 "	90/65	20			+150 ml. ml per se
	5 31	90/65	20			+150 ml. I ml per se
	5 32 "	90/65	20			
	5 34	90/65	30			
	5 40 "	100/70	40			
	6 20	100/60	110			
7	10 00 A.M.	120/80	100			+700 ml
	10 20	110/80	80			−200 ml.
	10 40	100/80	75			
	11 00	100/80	75			
	11 30	100/70	75			
	12 00 noon	110/60	110		84	+200 ml. I.A ml per sec
	12 10 P.M.	120/50	100		88	
	12 30	70/40			52	+200 ml. I.A ml per sec
	12 40	120/60			80	
	1 00	80/40			40	+200 ml. I ml. per se
	1 10 "	120/50			84	

On a few occasions when blood was not available a ɔid intravenous infusion of plasma was used in an empt to combat the effects of a sudden massive morrhage In those cases in which hypotension had ɔn severe and lasted for 5–6 hours the patients ponses to intravenous therapy were unsatisfactory In o particular instance the patient's condition was affected by the rapid intravenous administration of)0 ml of plasma An hour later 150 ml of blood was ven by the retrograde arterial route, whereupon there s an immediate and sustained rise in blood pressure th a fall in pulse rate. Plasma was not given intra erially, for reasons given below

Even with rapid rates of injection—e g 8 ml a second no sign of cardiac embarrassment was noted until the imated restoration of blood volume was complete ıen the pulse suddenly slowed the blood pressure fell nsiderably, and there was pronounced peripheral vaso atation These circulatory changes were reversed ontaneously and completely within 2–3 minutes after e transfusion had been stopped.

Plethysmographic Studies

As already stated, the response to intra-arterial trans sion usually appeared after a delay of 2–5 minutes In attempt to discover what was happening during this ent period, plethysmographic records were made from ı consecutive cases, and seven satisfactory plethysmo ams were obtained The three other tracings were scarded either because they were marred by technical ılts in the equipment or because severe circulatory sturbances had appeared as a result of interference with e basal structures of the brain

It was decided to estimate the blood flow through the ; and foot, although it was known that this method of easurement had been abandoned several years ago ıder conditions of altered blood volume the vessels of e skin, which is a large and not unimportant organ ust exert a considerable influence For the purpose of mparison the first two cases had simultaneous record gs made with the foot occluded and with the foot culation intact. The difference noted appeared to be ıe of degree rather than response.

Plethysmograms were recorded by the method scribed by Barcroft and Swan (1953)

sults

The results obtained in seven of the cases are set out the accompanying table Blood flows were estimated percentages of the initial blood flow

In one case, after a prolonged period of reactionary soconstriction, the plethysmogram altered from the ual triangular shape becoming trapezoidal in outline. his appearance coincided with the disappearance of ıe superficial veins, the normal triangular tracing appeared when the superficial veins began to be visible ıce more This alteration was not due to faulty record g but was probably due to a severe reduction of the ripheral vascular capacity brought about by intense soconstriction

Discussion

Retrograde arterial transfusion has been used success ılly in 105 cases Whereas intravenous and intra *rterial transfusions are equally effective in patients* who ıve suffered blood loss and hypotension for brief eriods, they differ when the latter conditions are more rolonged the patient failing to respond adequately) intravenous therapy A refractory state develops in hich there is a less satisfactory response to intravenous ıan to intra arterial infusions.

It may be asked why arterial transfusion should be ıccessful when intravenous therapy is not, and why the eaction to equal amounts of blood given by the two outes should differ both immediately and later

When oligæmic shock has developed after severe hæmorrhage, some patients show a satisfactory initial response to intravenous infusions, which however is maintained for only a few hours This happens even if the circulating blood volume has been restored to normal.

It appears that circulatory failure following severe hæmorrhage or injury has two components : a failure of vasoconstriction to compensate adequately for the reduced circulating blood volume and a "central factor" probably due to a failure of the heart to act as an efficient pump under normal conditions of venous return and filling pressure

In patients who have been temporarily resuscitated by adequate intravenous therapy the peripheral mechanism can still work for a reasonable circulation is maintained for several hours before the patient again passes into the state of circulatory failure.

Wiggers (1947) has shown that rapid intravenous transfusion is followed by an increase in venous return and cardiac output, but that the auricles and ventricles are considerably distended working under abnormal conditions of filling As the venous pressure falls after the transfusion is stopped, cardiac output declines, and so the patient again develops circulatory failure This is the *state of so-called irreversible shock and Wiggers showed* that the myocardium was significantly depressed The cardiac output was therefore reduced for a normal degree of filling and hence stimulation

In the less ill patient in whom circulatory failure is present but where successful resuscitation follows adequate intravenous transfusion, probably the "central" insufficiency has not yet developed to a serious degree. In this case the most important factor has been the inability of reactionary vasoconstriction to maintain an adequate circulation, because of an excessively reduced circulating blood volume, correction of which alone is sufficient to allow restoration of a normal circulation

In several published reports it has been postulated that retrograde arterial perfusion will raise the pressure in the arterial tree including the aorta, according to physical laws without having to presuppose any other less tangible theory This rise would lead to an increased coronary perfusion pressure, and accordingly improved *nutrition of the myocardium restoration of the efficiency* of the heart, and so correction of "central failure."

This suggestion by ignoring the vasodepressor responses from the aortic arch and the carotid arteries assumes that there is no alteration in peripheral resistance during transfusion for if there is any change, there may be no significant alteration in blood pressure.

No alteration in blood pressure during intra-arterial transfusion could be demonstrated in any of the cases under review apart from the very transient rise and fall of some 5 mm Hg at the start and end of the transfusion This minimal and extremely brief fluctuation hints at a readjustment in the operation of the vasomotor compensating mechanisms

Plethysmograms showed that the blood flow measured below the knee during the transfusion was increased 2–5 times, and that the flow returned to the pre transfusion level immediately the administration was stopped 2–3 minutes later the recordings indicated a progressively increasing blood flow before there was any change in blood pressure

The plethysmograms showed that there was a difference in the response to the administration of small quantities of blood between the intravenous and retrograde arterial routes, the response being greater and more prolonged after arterial transfusion Indeed after all but the shortest periods of reactionary vasoconstriction no response could be demonstrated after the intravenous administration of small quantities such as 100 ml., of fluid whether blood plasma, or other substitute

It will be appreciated that it is difficult to draw absolute conclusions from plethysmograms, but the interpretation of the tracings obtained, along with simultaneous blood pressure recordings, suggest that almost immediately after the initiation of arterial transfusion there is a decrease in the degree of peripheral vasoconstriction. Vascular tone returns to the pre-transfusion level immediately the injection of blood is terminated, to be followed within 2–3 minutes by a further decrease of vasoconstriction and, in the presence of an unaltered blood-pressure, an increase in cardiac output. A rise of blood-pressure only occurred several minutes after the first change in peripheral blood-flow had become apparent.

This response has usually been seen within 5 minutes of the end of the arterial transfusion, although in ten cases the response was less than anticipated. These latter were all cases in which a protracted period of severe hypotension had been maintained. With the giving of further quantities of blood over the next 10 minutes the circulation was permanently restored and maintained at an adequate level.

It has not been possible to demonstrate the mechanism whereby permanent resuscitation follows intra arterial transfusion whereas under equally critical conditions intravenous therapy produces only temporary improvement. It seems reasonably certain that the difference in results depends on restoration of the efficiency of the heart, and it is surprising that an intra arterial transfusion of 100–200 ml of blood, lasting only about 30 seconds, can initiate such a dramatic change. That a permanent change is brought about, however, is beyond dispute.

Dangers

Either arterial or venous “bank” blood may be used as the perfusing fluid. On one occasion 100 ml of physiological saline solution was injected, and the whole arm assumed a waxy hue from the finger tips to the axilla, nearly 5 minutes elapsed before a normal appearance returned to the limb.

To perfuse a limb with a non oxygen carrying fluid is to court disaster. Even in severe circulatory failure the patient's blood contains oxygen which is utilised by his tissues, but if plasma, saline, or other blood substitute is used, this solution will produce a rapid anoxia of the perfused tissues, which may be sufficient to cause local necrosis. This is probably of significance because all but two of the cases of gangrene published occurred after the use of plasma or of saline solution. Of the two exceptions, one case of gangrene was due to an anatomical abnormality in the arterial supply of the hand, there being no radial ulnar anastomosis, and the other was attributed to reflex spasm of the radial artery induced by the escape of blood into the tissues.

In the present cases the radial artery was routinely tied in continuity, the only complication met so far has been a mild blotching of the skin for a few hours over the area of distribution of the radial artery.

Conclusions

In civilian practice intra arterial transfusion should probably be restricted to the preoperative treatment of patients in whom there has been a considerable reduction of circulating blood volume and when there is no satisfactory response to intravenous therapy after a brief period of adequate trial.

Intra arterial transfusion is of value during those operations in which uncontrollable and massive hæmorrhage is likely—e g, in certain operations on the brain and the heart.

In military practice, when supplies of blood may be limited and time short, this method may be preferred to intravenous therapy, for it has been shown experimentally, as well as clinically, that a small quantity of blood
given by the retrograde arterial route has a vastly gr
effect than an equal amount of blood given intraveno
Once the desired effect has been achieved, the
transfusion can be discontinued, and plasma or
substitute administered intravenously to rest
patient's blood volume.

When the advantages of this method of treatm
suitably selected cases are compared with the disa
tages, the latter appear to be small. The risk of
following ligation of the radial artery at the wri
very slight, and to take such risk is justifiable in d
with cases in which life may depend upon the abili
resuscitate the patient.

In severe circulatory failure it is doubtful wheth
will take longer to expose and cannulate an artery
a vein shrunken and emptied by reactionary
Nevertheless it may be difficult to cannulate the r
artery under conditions of extreme vasoconstriction
occasionally it may be necessary to insert a needle
the femoral artery or even into the aorta.

We have never yet met conditions in which reactio
arterial spasm involving the limb prevented the inje
In those few cases in which there was difficulty
was restricted to a segment of the vessel about 2 cm.
at the site of insertion of the cannula. It was m
overcome by applying 2% procaine solution to
affected segment. Spasm is readily caused by
handling of the artery or as the result of using too
a transfusion pressure.

Summary

In the data collected from 165 cases there is
that intra arterial transfusion is of advantage in
treatment of patients who have become exsan
to critical levels, or are in severe circulatory f
other reasons, it is unnecessary and unjustifiable
the blood loss is small.

I am grateful to Prof Norman Dott for his
and assistance during this investigation, and to Dr
Gillies and Prof David Whitteridge for their help in
this study and for their valuable criticism in assessin
results.

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We look back with horror on the sufferings of p
even two or three generations ago, when we consider
much could have been relieved by modern anæsthesia
sedation, let alone the advances in surgery and therape
Yet we still tend to accept a host of minor disabilit
visitations of God—painful, embarrassing, irritating,
mentally depressing as the case may be—even when reme
are within reach. This applies especially to disabilit
the feet minor but intensely troublesome rheumatic condi
allergic manifestations of one kind and another, and
lesser psychoneurotic infirmities that respond so well to s
guidance and human understanding. We are in dang
repeating in our age of science the magnificent bathos of
as reported in the Book of Kings

> The rest of all the acts of Asa, and all his might, and al
> he did and the cities which he built are they not written
> book of the chronicles of the kings of Judah? Neverthele
> the time of his old age he was diseased in his feet.

This is still the outstanding fact of 1953 that the
vention of painful and crippling conditions of the feet
subject deserving studies of epidemiological dimens
—Prof J M MACKINTOSH *The Practitioner*, October, 1
p 440

HYALINE MEMBRANE IN THE NEONATAL LUNG

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E of the great dangers of early neonatal life is the re of the lungs to expand fully This failure may from the time of birth (primary atelectasis) or rying degree of expansion of the lungs may be wed by collapse (secondary atelectasis)

electasis, whether primary or secondary is very ently encountered in premature infants and is d the most important single cause of death among Though the use of antibiotics has greatly reduced prevalence and severity of respiratory infections in neonate, death from respiratory failure is still non in the premature infant The clinical features electasis neonatorum, and some methods now being ed to combat it have lately been described by ld and Lord (1953)

the pulmonary abnormalities found in association atelectasis in the newborn the most striking e presence of a hyaline membrane This peculiar brane was first noted by Hochheim (1903) and described more fully by Johnson and Meyer (1925) latter were chiefly interested in pneumonia in the orn and in the relation of this membrane to pul ary infection *There has been considerable con* n over its ætiology and significance and the subject viewed in detail by Tran Dinh De and Anderson 3)

view of the importance of atelectasis as a cause of h in the newborn, the development of a hyaline brane seemed to merit further investigation Accord I have reviewed the histological preparations from lungs of all infants examined post mortem at the n Charlotte s Maternity Hospital and Hammersmith pital in the five years 1948–52 inclusive In all, 2500 blocks of lung tissue have been studied.

Findings

INCIDENCE OF HYALINE MEMBRANE

ut of 810 necropsies on stillbirths and neonatal hs 108 cases were found to show hyaline membrane as then noted that none of the infants in which it rred had been stillborn The membrane had efore developed in 108 (29%) of 376 liveborn infants incidence similar to that reported by Bruns and lds (1951), Tregillus (1951) and Blystad et al. 1) Only Miller and his associates (1949 1950) reported hyaline membrane in stillbirths

f the 108 infants with hyaline membrane 76 were es and 32 females (male preponderance 2·4 1)

ELATION OF MEMBRANE TO MATURITY OF INFANT

he cases may be grouped according to their birth ghts as follows:

500–1000 g	12	2001–2500 g	15
1001–1500 g	36	Over 2500 g	22
1501–2000 g	23		
		Total	108

ill be seen that only 22 (20%) weighed 2500 g or r Thus hyaline membrane occurs chiefly in premature nts.

TIME AND CAUSE OF DEATH

he ages of the infants dying with membrane in the g were:

0–12 hours	44	37–48 hours	13
13–24 "	27	Over 48 "	12
25–36 "	12		
		Total	108

It will be seen that 71 (66%) died in the first 24 hours The earliest death was at $1^1/_2$ hours and the latest at $6^1/_2$ days 4 other infants lived for 6 days

The main causes of death were

Hyaline membrane only	81
Subdural hæmorrhage	9
Intraventricular hæmorrhage	7
Hæmolytic disease	5
Pneumonia	4
Intrapulmonary hæmorrhage	1
Hydrocephalus	1
Total	108

Hyaline membrane was the sole pathological lesion in 81 cases (75%) Intracranial (subdural) and intra ventricular hæmorrhage were the next commonest causes Intraventricular hæmorrhage is not infrequently asso ciated with atelectasis and the formation of hyaline membrane It is to be regarded as the result of anoxia rather than of birth trauma There were only 4 cases of pneumonia. Of the 22 infants weighing 2500 g or more, 7 were postmature, 4 were delivered by cæsarean section, 3 suffered from hæmolytic disease 1 had hydro cephalus, and 6 had severe subdural hæmorrhage follow ing difficult forceps deliveries Thus 10 (45%) had some pathological disorder 4 (18%) were delivered by section and only 1 had a normal gestation and delivery Although this group of 22 infants were not subject to the hazards of prematurity they could not be regarded as normal healthy infants at the time when hyaline membrane was formed

INCIDENCE OF CÆSAREAN SECTION

As Potter (1952) has remarked hyaline membrane often occurs in infants delivered by cæsarean section *In the present series of 108 cases 22 infants* (20%) were delivered by section The period of gestation at which section was carried out, and the reason for the section are shown in the accompanying table The 4 infants weighing over 2500 g were delivered by section at 38 weeks By far the most important reason for section was severe pre-eclamptic toxæmia—13 cases (59%) Ante partum hæmorrhage with or without placenta prævia accounted for another 5 cases (23%) One in every five of the hyaline-membrane cases had been delivered by cæsarean section

CÆSAREAN SECTION

Reason for section	No	Period of gestation	No
Pre-eclamptic toxæmia	13	20–30 weeks	5
Antepartum hæmorrhage	2	31–34 weeks	11
Placenta prævia	3	35–38 weeks	5
Diabetes	3	Term	1
Contracted pelvis	1		
Total	22	Total	22

ABNORMALITIES IN THE MOTHER

There were 104 mothers of the 108 affected infants There were 4 pairs of twins and 14 other twins whose partners survived Thus twin pregnancy occurred in 18 of the 104 pregnancies (17%) There was one triplet in the series 31 (28%) of the mothers were primi parous The pregnancy had been terminated in 8 cases by artificial rupture of the membranes In 7 cases forceps delivery had been carried out and in 6 of these severe subdural hæmorrhage had occurred in the infant External version before delivery had been done in 2 cases. The presentation was vertex in 69 cases and breech in 17 the remainder being delivered by section

If multiple pregnancy is regarded as abnormal there was some abnormality during pregnancy in 69 women (66%)

In addition to the 19 instances of multiple pregnancy there were 19 cases (18%) of pre-eclamptic toxæmia. There were 11 cases of antepartum hæmorrhage and 5 cases of rhesus iso immunisation There were 3 cases of severe heart-disease (1 of mitral stenosis 1 of paroxysmal tachycardia and 1 of patent ductus arteriosus) In 3 patients who came to premature labour there had been a threatened abortion earlier in preg

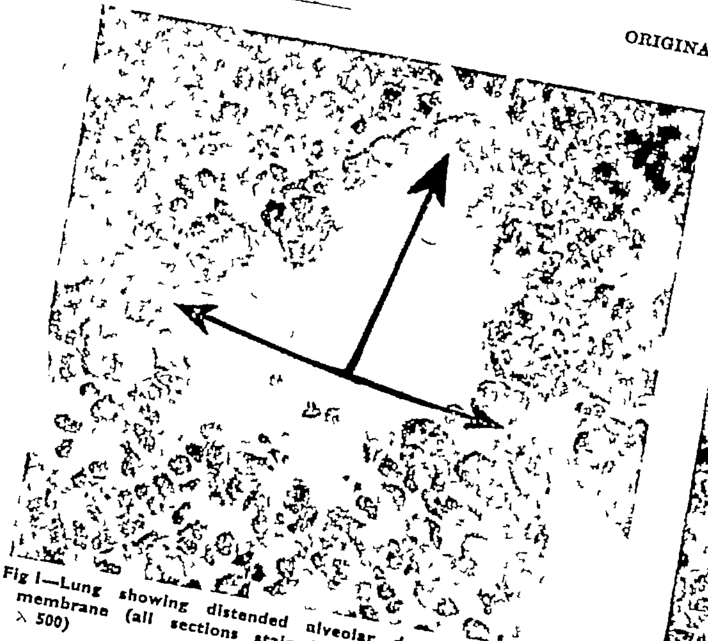


Fig 1—Lung showing distended alveolar duct lined by hyaline membrane (all sections stained with hæmatoxylin and eosin × 500)

nancy (2 at 8–12 weeks and one at 16 weeks) There were 3 cases of diabetes, 2 of bicornuate uterus, 2 of tuberculosis, 1 of syphilis, and 1 of nephrosis

ILLNESS IN THE INFANT

The clinical features of hyaline membrane formation have been fully described by Donald and Lord (1953) The infant is usually premature and there may be some difficulty in establishing respiration The air entry is poor and after an hour or two marked rib-recession develops There are cyanotic attacks and periods of apnœa, and the infant dies within 24–48 hours of birth

PATHOLOGICAL CHANGES IN THE LUNGS

On naked eye examination the lungs are bulky and dark red They show little evidence of aeration, and both lungs and each of their lobes usually sink when placed in water On being sliced, the lungs are seen to be airless, congested, and of the consistence of liver

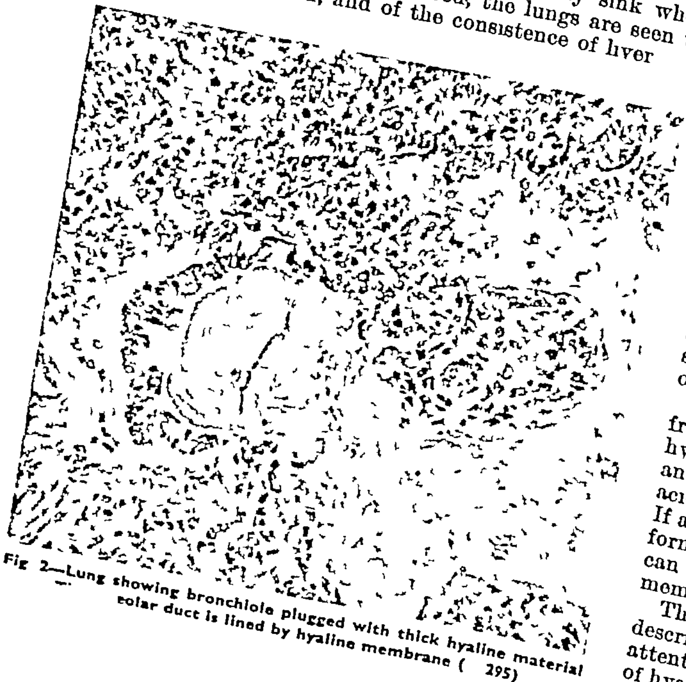


Fig 2—Lung showing bronchiole plugged with thick hyaline material eolar duct is lined by hyaline membrane (× 295)

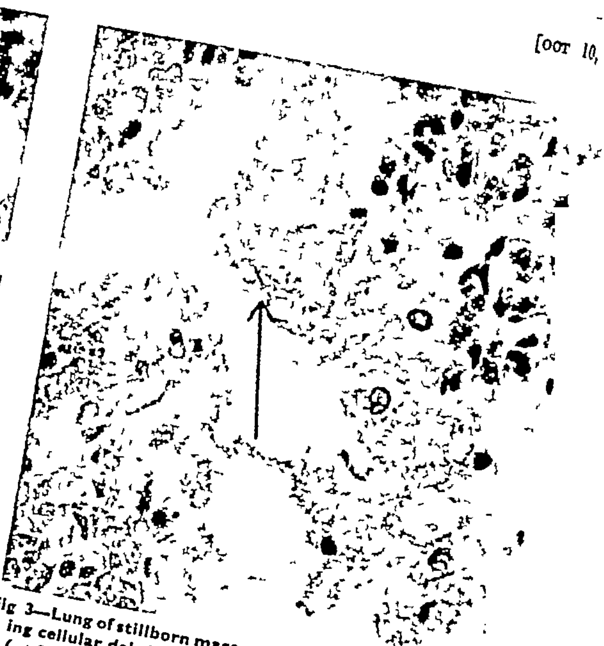


Fig 3—Lung of stillborn macerated fœtus showing alveolar du ing cellular debris and triangular plug of acidophil hyalin (× 380)

When examined histologically, the lungs have a appearance The greater part of the parenchym collapsed and the alveolar capillaries are eng Alternating with these atelectatic areas are a numb structures which appear to be overdistended Thes mainly alveolar ducts and respiratory bronch On closer examination these ducts and bronch are seen to be lined by dense hyaline material wh strongly acidophil when sections are stained hæmatoxylin and eosin This is the so-called hy membrane (fig 1) It is found chiefly lining ducts but also along the walls of some alveoli a bronchioles It does not stain for fibrin and weakly positive reaction with the periodic aci technique indicating the presence of a polysacc Often, but not always, neutral fat can be detec this membrane In spite of the use of a wide of special stains, the exact histochemical nature of hyaline membrane has not yet been determined

A study was made of some 450 blocks of lung t obtained from the 108 cases It was quickly re that the membrane is not quite so homogeneous i sections as was once thought In nearly ever some of the sections showed areas where the memb was less evenly distributed round the walls of ducts or was fragmentary The membrane ir areas seemed to be in process of formation and noticeable that it had a more precise structure less homogeneous than the fully formed materia seemed to be *cellular* In hæmatoxylin and sections the cells were bright red, and the faint o of a nucleus could sometimes be made out

The cells were then identified as flat squames from the liquor amnii Groups of these hyaline cells clump together, lose their cellular and cellular identity, and fuse to form the acidophil membrane lining the air spaces in the If a sufficient number of blocks are taken this progres formation of hyaline membrane from individual squ can be traced in nearly every lung containing h membrane

The transition from squames to membrane described by Johnson and Meyer in 1925, but attention has been paid to this aspect of the path of hyaline membrane More recently Miller and Ham (1949) noted the presence of certain cells in the neigh d of developing hyaline membrane They believed t these cells were responsible for the membrane nation but were unable to identify them Since the s were bright red and not basophil they rejected the that they might be squames from the liquor amnii my opinion, however they are indeed squames ch have become progressively more acidophil and line while lying in the air-spaces of the affected lungs n a number of cases plugs of hyaline acidophil terial are found in some of the alveolar ducts and piratory bronchioles (fig 2) These plugs are formed the fusion of groups of hyalinising squames but not dispersed round the walls of the air spaces in the n of membrane Nuclear remnants can sometimes identified These plugs may be very large, and directly blocking the airways they may be partly onsible for atelectasis The process of hyalinisation squames is not confined to liveborn infants small gs of similar material may be found even in the cerated fœtus (fig 3) Membrane formation does occur before birth, however because there is no air to perse the squames to the periphery of the air-spaces astly, typical cornified cells derived from the liquor nii can be found in most sections. These may be ttered in the lumen of the alveolar ducts and alveoli may be caught in the membrane itself They do seem to fuse into amorphous masses like the hyalinised ames. This may be because they are keratinised l cannot undergo the chemical change necessary complete hyalinisation

EXPERIMENTS

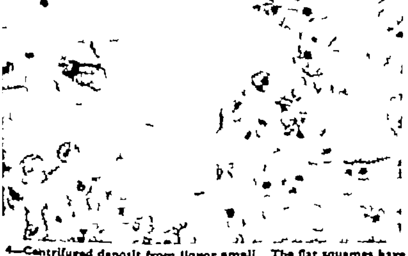
hese histological findings suggested that the primary tor in the production of hyaline membrane is aspiration iquor amnii

o substantiate this explanation samples of liquor nii were examined by chemical and histological thods An attempt was made to reproduce hyalinisa n in vitro And finally the reproduction of a hyaline mbrane in an animal was achieved

EXAMINATION OF SAMPLES OF LIQUOR AMNII

total of 40 specimens from separate pregnancies s examined.

6 of these specimens were obtained at term 10 were from t mature pregnancies and 4 were from premature deliveries. The amount of fluid in each specimen varied greatly for some of the specimens were from cases of hydramnios and 4000 ml or more was obtained Each specimen was centrifuged and the amount of sediment measured This amount varied from 0·1% to 7 2% by volume (average 1 9%): at 14 weeks and 25 weeks it was 0 1% and at 32 weeks it was 0 4%, indicating that the amount of solid material increased greatly as pregnancy advanced. This was as expected The protein content of the supernatant fluid was estimated. This varied from 40 to 300 mg per 100 ml with an average of 128 mg


4—Centrifuged deposit from liquor amnii The flat squames have faintly basophil cytoplasm and dark-blue central nucleus (× 300)

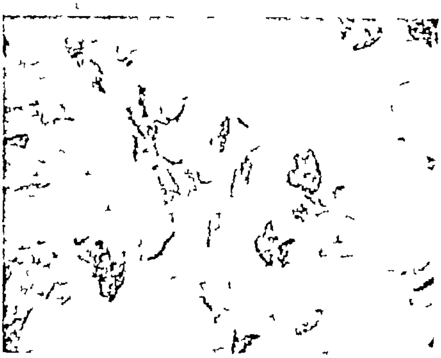


Fig 5—Centrifuged deposit from liquor amnii after 8 days incubation. Cells are more acidophil and nuclei have been lost (× 300)

Smears of the centrifuged deposit were fixed in alcohol and stained with hæmatoxylin and eosin The solid material was seen to consist of innumerable large flat squames which had a slightly basophil cytoplasm and a large dark central nucleus (fig 4) Varying numbers of cornified cells were also present. Paraffin sections of the centrifuged deposit had an appearance similar to that of the smears.

To simulate the hyalinisation which seemed to occur in the infants lungs samples of centrifuged liquor deposit were resuspended in an equal volume of saline and incubated at 37 C After 7–10 days the squames had lost their nuclei and had become strongly acidophil (fig 5) Some of the cells had coalesced to form hyaline masses not unlike those found in lung sections The incubated material now seemed to be in a favourable state for the production of a hyaline membrane and further experiments were made

EXPERIMENTAL PRODUCTION OF A HYALINE MEMBRANE

During the above investigation it was noted that some samples of liquor amnii did not centrifuge well, and that the supernatant fluid contained opaque tenacious white material This material contained numerous cornified cells but few flat squames, and this type of liquor was judged unsuitable for experiments

When a favourable sample of liquor amnii had been obtained by high artificial rupture of the membranes under aseptic conditions, the fluid was centrifuged Aliquot parts of the deposit were resuspended in equal volumes of sterile normal saline to which chloramphenicol 65 µg per ml. had been added. The suspensions were then incubated at 37°C for 8 days At the end of the incubation period smears were examined to make sure that hyalinisation of the squames had occurred The suspensions were then centrifuged and the deposit carefully ground in a sterile virus grinder to secure a completely smooth suspension To 0 5 ml of this deposit was added 0 5 ml sterile saline containing chloramphenicol 65 µg per ml. This material was then injected intratracheally into six young albino rats (weight 175 g) A further rat received an intratracheal injection of 1 ml sterile suspension of the deposit from the same fluid, but the deposit in this case had not been incubated

The rats which had received the injection of incubated material were killed at 1, 2, 3, 5, 24, and 29 hours The seventh rat was killed after 24 hours

RAT 1 (killed at 1 hour) —Hyaline material and some cornified cells were plugging the bronchi and bronchioles There was moderate collapse in the upper lobe of the right lung which was chiefly affected Some of the alveolar ducts were lined with hyaline material

RAT 2 (killed at 2 hours) —Hyaline material was seen in bronchi and bronchioles with a varying degree of atelectasis of the surrounding lung parenchyma Many alveolar ducts were lined by acidophil hyaline material which was forming a membrane Some cornified cells were seen in many areas

RAT 3 (killed at 3 hours) —Many bronchioles were plugged by acidophil hyaline material (fig 6) There was severe collapse of the surrounding lung parenchyma, especially in the upper lobe of the right lung where areas of collapse were evident on naked eye examination Some overdistended alveolar ducts were seen to be lined by acidophil hyaline membrane (fig 7) This membrane was exactly comparable to that found in the lung of an infant (fig 1) A moderate polymorphonuclear leucocyte reaction was observed in some areas

RAT 4 (killed at 5 hours) —The injection had been unsatisfactory and only scattered clumps of hyaline material and cornified cells were found

RATS 5 AND 6 (killed at 24 and 29 hours) —Findings as in rat 3 The increased duration of the experiment had little or no effect on the outcome

RAT 7 (killed at 24 hours) —This rat received the material which had not been incubated No areas of collapse were evident macroscopically Histologically a few small atelectatic areas were present Many bronchioles were plugged with cornified cells and similar cells were present in neighbouring alveoli There was some overdistension of alveolar ducts in the collapsed areas and occasional collections of cornified cells against the duct walls These bore a faint resemblance to hyaline membrane, but such aggregations were very small and the picture was in no way comparable to that found in rat 3

This experiment showed that suitable treated deposit from the liquor amnii will produce an acidophil hyaline membrane when injected intratracheally into a rat. membrane thus formed lines bronchioles and al ducts in the same manner as the membrane found lungs of infants It is acidophil with hæmato and eosin staining, and fat droplets were seen in th sections stained with Scharlach R

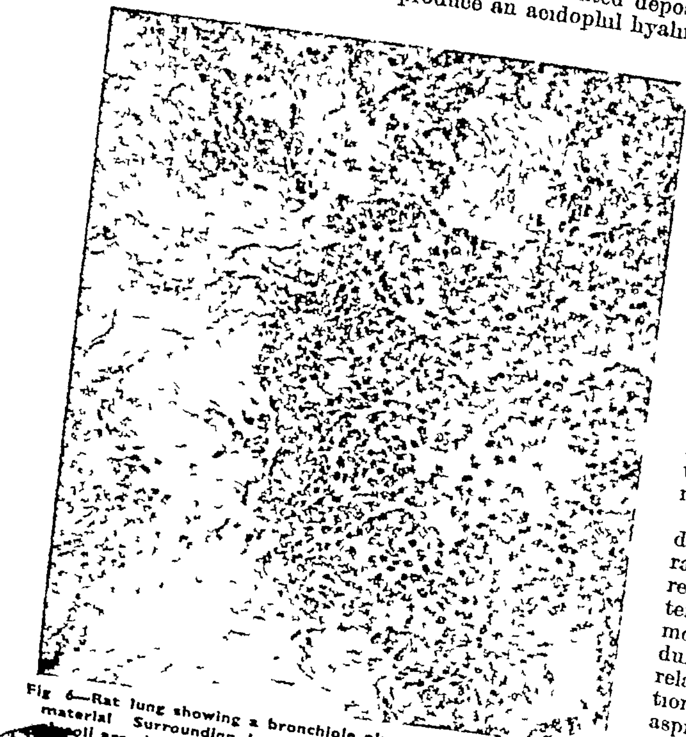


Fig 6—Rat lung showing a bronchiole plugged by acidophil hyaline material Surrounding lung is completely collapsed and some alveoli are also plugged with this material (× 340)

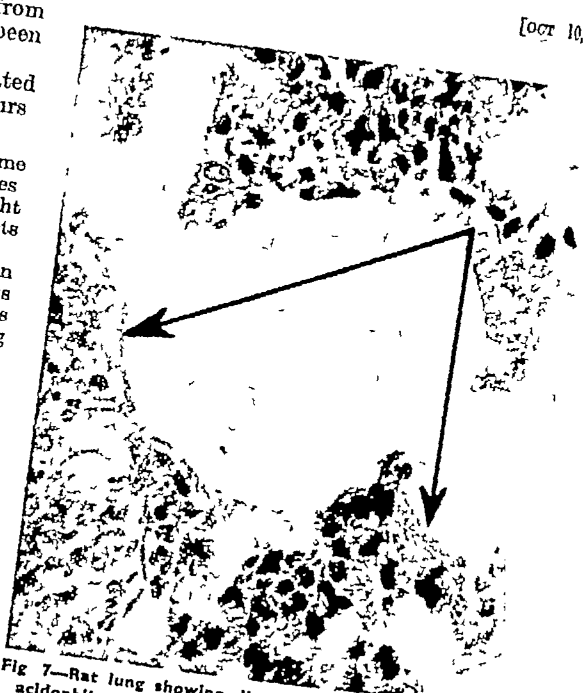


Fig 7—Rat lung showing distended alveolar duct partially acidophilic hyaline membrane Surrounding lung is collaps few of the alveoli contain plugs of acidophil material (× 34

Discussion

In this survey of 108 cases of hyaline membrane fo tion the majority of affected infants were p a finding similar to that of other workers Of affected infants who were born at term or post ma the majority had some other pathological lesion subdural hæmorrhage or hæmolytic disease) which them, like premature infants, less able to deal aspirated liquor amnii Moreover, circumstances sometimes have led to their inspiring an unduly quantity of liquor For example, it is well known t as the infant is extracted from the uterus by section it is inclined to take a gulp of liquor and we may note that of the 108 infants in this 22 were delivered by section, but it is only fair t out that 16 of these (73%) were delivered bef 35th week and so were premature

It has also been pointed out that 50 of the m had some abnormality of pregnancy—the being pre eclamptic toxæmia—and that a furthe had a multiple pregnancy These abnormalities to increase the risk of premature delivery and thus risk of developing a pulmonary hyaline membrane

The reason why premature infants are more pro develop this membrane than mature infants re rather obscure It is possible that the premature inf respiratory centre is more sensitive to changes in o tension and that intra uterine respiratory efforts o more easily In response to anoxia, either before during delivery, the premature infant may as relatively large quantities of liquor amnii The cu tion in the premature infant's lung is less able to al aspirated fluid than is the mature infant's and squames deposited in the air passages are in fact incub in a fluid medium which allows hyalinisation to p When the infant is delivered and begins to bre the hyalinised material is dispersed round the he air passages in the form of a membrane It is possible that the liquor amnii at 28–36 weeks ation contains a relatively high proportion of non tinised squames which are unusually susceptible to process of hyalinisation This possibility requires her investigation.

fter aspiration the squames deposited in the lung ergo progressive hyalinisation This may be well anced by the time the infant is delivered since nbrane formation has been detected in an infant ng $1\frac{1}{2}$ hours after birth

arber and Sweet (1931) suggested that the membrane formed as a result of aspiration of vernix caseosa e it gave a positive reaction for fat. But in fact ny hyaline membranes contain little or no fat If any given case the squames involved in membrane nation are derived from vernix and covered with fat n, and then only will the membrane give a positive tion with fat stains This explains the varying ilts from case to case where fat stains are employed

lystad et al (1951) suggest that the liquor is absorbed the lung of the newborn infant but the protein is left ind in the air-spaces as this protein gradually centrates, it is laid down as a membrane lining the ls of alveoli and alveolar ducts It is probable that h concentration of protein does occur, and that it s to the thickness of a membrane already formed by hyalinisation of squames It is unlikely to be respon e for the formation of the entire membrane which is n very thick

telectasis is the cause of the infant's death In the eriment on rats the atelectasis was largely the result plugging of the respiratory bronchioles and mouths of eolar ducts with thick hyaline material In the infant mechanism is also at work but other factors are also olved. In the infant's lung hyaline membrane is ch more widespread than any yet produced in the erimental animal. (This is partly because the infant utero can aspirate fluid into all branches of the nchial tree whereas a corresponding injection of d into the bronchial tree of rats would probably ult in rapid death from asphyxia.) The membrane ering numerous alveolar ducts in the infant's lung erferes with the gaseous exchange and prevents air ching the more distal air-spaces which become npletely collapsed But at birth the hyaline material probably not in the form of a membrane and air is e to reach the distal alveoli The pressure of air forces material against the walls of bronchioles and alveolar ts and this eventually seals off the distal air-sacs s explains how some infants seem to breathe reason y well shortly after birth but their respiration omes progressively more laboured until death ensues

he present study indicates that massive aspiration liquor amnii is the prelude to formation of hyaline mbrane. The infants thus succumb to an unusual form drowning While the fluid is largely absorbed into the lmonary circulation, the mud left behind in the form hyalinised squames eventually covers the walls of the eolar ducts and leads to death by suffocation

Summary

Hyaline membrane was found in the lungs of 108 t of 370 liveborn infants who died in the early neonatal riod.

It is suggested that this membrane is formed from uames in the liquor amnii The liquor is aspirated o the fœtal lung and the squames undergo progressive alinisation and fusion

Suitably treated deposit from human liquor amnii, ien injected intratracheally into the rat, will produce hyaline membrane in the animal's lung

The atelectasis associated with hyaline membrane in e newborn infant is partly the result of direct obstruction of the airways by plugs of hyaline material and partly the result of air being trapped in the distal air-sacs when the alveolar ducts are sealed by membrane

I am indebted to Dr J Murray for much advice and criticism I wish to thank Dr G H Lathe and his staff for undertaking the chemical investigations and for considerable help with the experiments. I am grateful to Mr Ian Donald for much coöperation on the clinical and physiological aspects of this work, and to the obstetric staffs of Queen Charlotte's and Hammersmith Hospitals for obtaining samples of liquor amnii The photomicrographs were prepared by Mr E Clark of Queen Charlotte's Hospital

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GASTRIC RESECTION

FOR GASTRODUODENAL HÆMORRHAGE WITHOUT AN OBVIOUS ULCER

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Now that surgery plays an increasing part in the management of the bleeding ulcer a new problem has been added to those which the surgeon has to solve during the course of operation. In some cases thorough inspection and palpation of the stomach and duodenum reveals no ulcer and in the absence of any other obvious cause of hæmorrhage the surgeon has to decide whether to operate further or to close the abdomen, as in the four following cases

Case records

Case 1—A woman aged 20 with two years history of epigastric pain coming on an hour after food and relieved by alkalis, was admitted with hæmatemesis pulse-rate 88 blood pressure 125/70 mm Hg and Hb 85% She had another hæmatemesis next day and a blood transfusion of two pints. Four days later bleeding recurred, and her pulse rate was 120 blood pressure 115/60 mm. Hg and Hb 56%

At laparotomy no ulcer was found. Gastrotomy revealed bleeding from multiple small acute erosions In view of the patient's age gastric resection was not considered advisable Two pints of blood was given during the operation. Eight days later the Hb was 56% and the patient was given two pints of blood She was discharged on the eighteenth day after operation.

Case 2—A man aged 53 who had had epigastric pain 1–$1\frac{1}{2}$ hours after food for three weeks had a hæmatemesis. His pulse rate was 70 blood pressure 110/70 mm. Hg and Hb 38% He was given a blood transfusion of three pints Bleeding recurred four days later and he was given three pints of blood and prepared for operation during which two further pints was transfused

At laparotomy no ulcer was found. Partial gastrectomy was done and the patient made an uneventful recovery Dr James McMurray reported on the operation specimen as follows Specimen of lower part of stomach shows acute gastritis, most marked in the prepyloric zone The microscopical preparation shows acute inflammatory change involving mucosa, submucosa, and muscle There is also much fibrosis in the submucosal layer with diffuse chronic inflammatory cell infiltration of mucosa and submucosa. The stomach wall is intensely engorged with blood and is œdematous. The findings indicate acute gastritis superimposed on chronic gastritis.

Case 3—A man aged 77 with no obtainable history was admitted collapsed, pale and dyspnœic with pulse rate 124, blood pressure 115/45 mm Hg, and Hb 26%. Three pints of blood was given. Next day his Hb was 35%, and he was given a blood transfusion of two pints. Two days later a melæna stool was obtained on digital examination of the rectum. Although a further three pints of blood had been given the Hb was 43%. Preoperatively and during operation three more pints of blood was given.

At laparotomy no ulcer was found. Gastrotomy was not done. The patient died three days later. Dr James McMurray reported: "The stomach mucosa shows much autolysis. There are two ulcers on the posterior wall about the mid third of the stomach. One is large (2 × ½ in.) and ellipsoid in outline. The other is small (¼ in.). Both show ulceration down to the muscle layer. A small artery protrudes at the edge of the larger ulcer and is the probable source of bleeding."

Case 4.—A woman, aged 73, known to be hypertensive and subject to epigastric pain after food for two years, had a hæmatemesis. Her pulse rate was 108, blood pressure 104/50 mm Hg, and Hb 50%. She was given a blood transfusion of three pints. Two days later she passed bright blood in a melæna stool. She then had a pulse rate of 102, blood pressure 100/50 mm Hg, and Hb 40%. She was transfused with the cells of four pints of blood.

At laparotomy no ulcer was seen. Partial gastrectomy was done, and the patient recovered. The operative specimen contained a large ulcer, 1½ × ¾ in., down to, but not involving, the muscle layer.

Comments

Case 1 was the only one in which gastrotomy was done. When the lesion was revealed a decision against gastric resection was made in view of the patient's youth. She made a good recovery and required only a further two pints of blood between operation and discharge from hospital. However, these cases are not always so uneventful. Tanner (1950) reported a similar case in a man, aged 26, with hæmorrhage from erosive gastritis, in whom bleeding continued after ligation of the right and left gastric and right and left gastro-epiploic arteries and partial gastrectomy became necessary.

The pathology in the specimen removed from case 2 was identical with that of case 1. In case 2, however, gastrotomy had not been done, partial gastrectomy being undertaken though no ulcer was found. In view of this patient's age I believe that this treatment is correct, and I would have gone on to this operation if gastrotomy had revealed the lesion.

In case 3 gastrotomy would possibly have disclosed the ulcer, because the stomach did not contain blood-clot; but in my opinion the error was in not proceeding to partial gastrectomy notwithstanding the lack of an obvious ulcer. The patient was a very poor surgical risk, and it is doubtful if his life could have been saved; nevertheless he did not receive the benefits of adequate surgery. Case 4 had an identical lesion, again not detectable on inspection and palpation, but with case 3 in mind gastric resection was done, and the result of examination of the specimen amply justified this action.

Discussion

In dealing with patients aged more than 50 and n the absence of any other causal lesion, opinion is ncreasingly in favour of partial gastrectomy if no lcer is found at emergency operation for hæmatemesis r melæna. The surgeon has, however, two other ossible courses of action, gastrotomy or merely to close e abdomen.

The value of gastrotomy is very variable; I have nd it of little value, because it is difficult to examine entire mucous surface of the stomach, especially he presence of blood-clot, which adheres to the stomach l and proves difficult to remove sufficiently thoroughly ve a complete view. Ogilvie et al (1952) write: "Incision of the stomach and duodenal wall and search e the viscus is an unsatisfactory procedure, for it is le to search adequately all the large potential area of bleeding; and the slender prospect of a positive r does not justify the soiling and further loss of blood that method entails."

Closure of the abdomen without further as in case 3, is futile; the patient has been put to t risk of operation but denied the possibility of ben from it. Bleeding ulcers are responsible for ab 90% of massive intestinal hæmorrhages, and in th cases in which operation is considered necessary if lesion is found gastric resection holds the best hope recovery. Ogilvie et al report having done par gastrectomy on seven patients in whom no ulc found; the specimens revealed shallow ulcers or m erosions. Downie (1952) reported six similar Tanner (1950) states:

"If bleeding is of really great severity, and no l is found, then gastrectomy is advisable, for it removes f fifths of the erosive area and partially devascularises remnant."

Ives (1949) asserts that in these circumstances gas-tomy provides no guarantee that an ulcer may not missed, that simply to close the abdomen is a counsel despair, and that a high partial gastrectomy is t correct procedure. My experience confirms the val of these conclusions.

Conclusions

Partial gastrectomy is the operation of choice i emergency laparotomy for hæmatemesis or melæna causal lesion, ulcer or other, is found in a patient more than 50.

Gastrotomy is not very helpful. It is unnec in patients aged more than 50, for whom gastrect should be done. In young patients, as in case 1 repor here, gastrotomy may be of value in deciding ag gastric resection, but note must be taken of the reported by Tanner (1950) and cited above.

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CONTROLLED HYPOTENSION WITH ARFONAD IN NEUROSURGERY WITH SPECIAL REFERENCE TO VASCULA LESIONS

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SINCE the methonium compounds were introd into anæsthetic practice by Enderby (1950) and Dav (1950) there has been much controversy about th use. It is our view that induced hypotension h not only made possible neurosurgical operations wh could not otherwise be attempted because of obscurati of the operation site by bleeding but also reduces risk of certain intracranial operations.

By the use of hypotensive drugs at operation, cranial pressure can be lowered, thereby diminis the risk of brain damage by herniation through dural opening. A further advantage is gained reducing the operating time, the amount of anæsth required, and blood loss. In the improved operat conditions surgical trauma is lessened. Recovery fr surgery is also quicker.

ough possessing the above mentioned advantages iethonium compounds are lacking in one important ct :– the blood pressure cannot be quickly raised hen lowered again at will The initial fall in blood ure may be greater than that needed in the pre- ary stages of surgery, whilst at a later stage it may impossible to lower the blood pressure quickly emand to the level required by the surgeon at a cular moment for a specific purpose It seems as gh a tolerance to the methonium compounds lops, with the result that, after the initial dose ited injections have less effect The use of procaine e together with hexamethonium bromide (Mason Pelmore 1953, Ascrman 1953) overcomes this ulty to some extent.

hen *Magill et al (1953) reported on the use of the* -acting hypotensive agent Arfonad it seemed able that this drug might produce better control e blood pressure than did the methonium compounds urable reports on the use of arfonad in surgery were published by Nicholson et al (1953) and Sadove . (1953)

perimentally produced acute toxicity varies accord o the route of administration and the species of al used (Randall et al 1949)

March 1953 we obtained a supply of arfonad for Our conclusions concerning its value are based 2 craniotomies done during hypotension induced it. These operations were done for intracranial ders which can be classified as follows

		Anæsthetists				
		S.A	*D.A*	*D.B*	*C.S*	*E.dell*
scular abnormalities						
neurysm	9 cases	6	0	2	0	1
ngioma	8 cases	2	3	1	1	1
ningioma	9 cases	2	6	1	0	0
oma	13 cases	6	5	1	0	1
scellaneous	13 cases	2	10	0	0	1

fonad is a vasodepressor with ganglion blocking and t vasodilator activity Its chemical name is *d* 3, 3 -dibenzyl 2 ketoimidazolido) 1 2 trimethylene phanium *d*-camphor sulfonate

Technique of Administration

ie method of administration we now use is as ws

ter induction with thiopentone used with a relaxant ation is done and an intravenous drip set up The l pressure is recorded The table is now tilted into 30 reverse Trendelenburg position About two minutes the blood pressure is again recorded Blood pressure ation after tilting is of great importance because the n pressure is very variable : and it is a valuable guide o amount of hypotensive drug required. After the scalp been cleaned the arfonad drip is started at first slowly nable the patient s reaction to be observed For the ing stages a systolic pressure of about 80 mm. Hg is idered enough to reduce hæmorrhage

hen the dura has been opened, the pressure is further red (to 60–70 mm. Hg) thereby diminishing intra ial tension and the surgeon s difficulties The blood ure is maintained at this level unless and until a demand ade to decrease it further—e.g., at the moment of excising neurysm

the later stages of operation before the dura is closed blood pressure is returned to near normal or at any rate 00 mm Hg by stopping the infusion and levelling the By so doing the bleeding points are seen and controlled the risk of postoperative blood clot formation is reduced the final stages, but only after replacement of the flap so that extradural bleeding points can be rved and controlled the blood pressure is again lowered bout 80 mm. Hg to prevent blood loss from the skin

naesthesia is maintained with nitrous oxide and gen supplemented by intravenous pethidine. Small es of relaxants are also given if coughing is anticipated

Results

Hæmorrhage

During operation.—In only 2 of the 52 craniotomies was blood loss sufficient to warrant blood transfusion In the 1st case a large suprasellar meningioma was removed which produced *bleeding from the internal* carotid artery The 2nd case was in an infant aged 18 months, subjected to hemispherectomy Of the 17 craniotomies done for cerebrovascular abnormalities 9 were for aneurysm In very few of these cases would radical surgery have been possible without some form of induced hypotension None of these cases required blood transfusion The remaining 8 operations were for angioma all of which would probably have required blood transfusion before the advent of hypotensive techniques as would most of the cases with meningiomas.

Postoperative hæmorrhage.—In 2 cases within forty eight hours of craniotomy the wound had to be reopened for removal of postoperative blood-clot The incidence of this complication is not high Both of these cases occurred before the precaution was observed of raising the blood pressure to normal and arresting all extradural bleeding before replacement of the bone flap In the last 30 cases since this procedure has been adopted as a routine no postoperative clot has been observed

Operative Mortality

Of these 52 patients undergoing major craniotomy 4 died after the operation ; 3 with meningiomata died within forty-eight hours of the operation ; and 1 patient who had an anterior communicating aneurysm and was bleeding at the time of operation died on the tenth postoperative day from surgical occlusion of both anterior *cerebral arteries In all of the 3 fatal cases of meningioma* there was a very large suprasellar tumour extending backwards into the middle fossa and the hypothalamic region 1 of them had been considered inoperable in another hospital and was attempted at the express wish of the relations In each case a major blood vessel (in 2 the internal carotid artery and in 1 the middle cerebral artery) was damaged and had to be clipped These 3 patients were women aged 72, 62 and 55 and poor subjects for such severe operations

In none of these cases was there reason to believe that induced hypotension played any part in the fatal outcome.

Failure to Induce Hypotension

All the patients to whom arfonad was administered responded by a fall in blood pressure In 1 case only was there failure to lower the blood pressure to the level required by the surgeon nevertheless very adequate

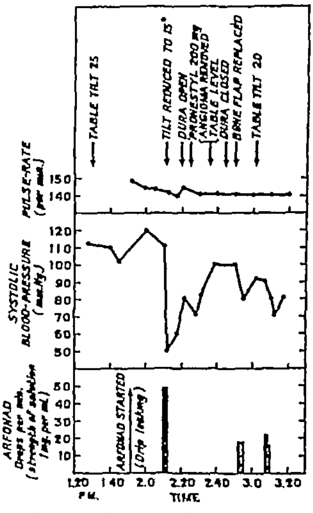

Fig 1—Observations on a child aged 6 ½ years undergoing craniotomy for removal of a posterior parietal angioma. Response was at first unsatisfactory because the drip was "leaking"

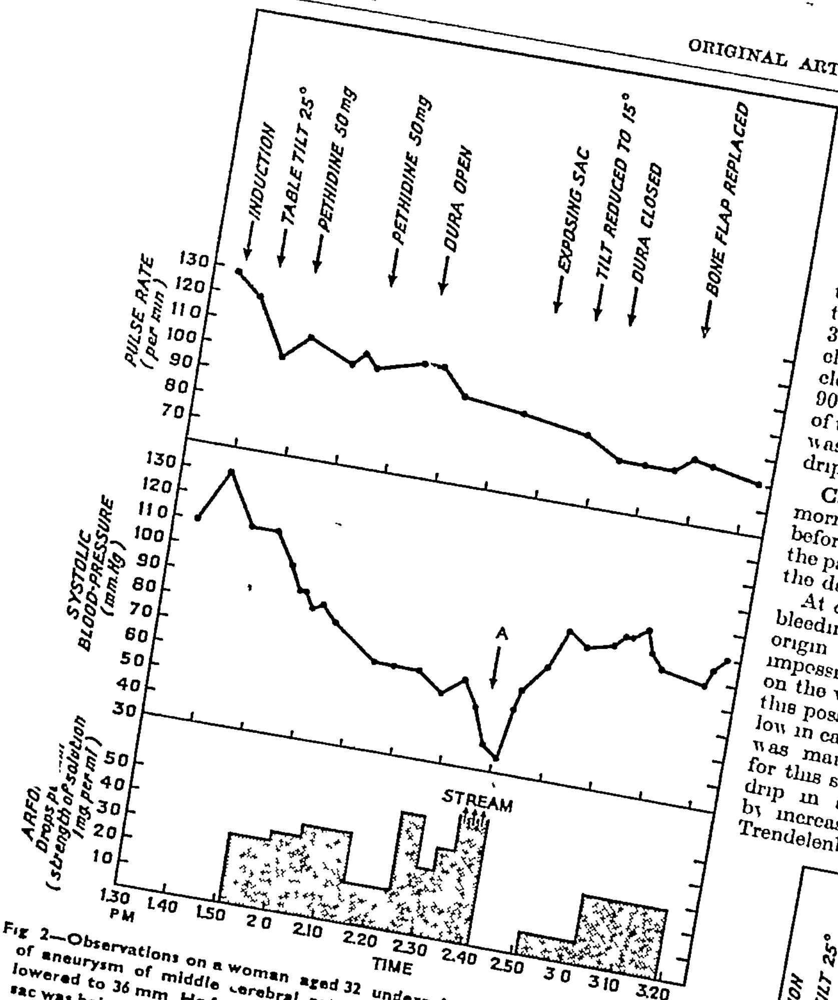

Fig 2—Observations on a woman aged 32 undergoing craniotomy for excision of aneurysm of middle cerebral artery The systolic blood pressure was lowered to 36 mm Hg for two minutes (A) while the neck of the aneurysmal sac was being closed

operating conditions were provided by maintaining the patient's blood pressure at 80 mm Hg

Failure to Maintain Hypotension

After the blood pressure had fallen, the hypotensive state was easily maintained In 2 cases only was it necessary to supplement the arfonad with procaine amide in case 3 to keep the blood-pressure unusually low, and in case 1, a girl aged 6½ years, to lower the pulse rate (see below)

Failure to Restore Blood pressure

Although arfonad is short acting, the blood pressure was seldom restored as soon as the infusion was stopped There was usually a lapse of 1–20 minutes This disadvantage, with 2 exceptions, was overcome by flattening the table In 2 cases 'Methedrine' 5 mg was injected to hasten the return of blood pressure to normal

Illustrative Case-records

Case 1—A girl aged 6½ years had four intracerebral hæmorrhages during the past two years Carotid arteriography showed what proved to be an angioma in the parieto-occipital region At 1 52 P.M the arfonad drip was started (fig 1) After three minutes the systolic blood pressure had risen from 102 mm to 120 mm Hg and the patient was coughing It was then realised that the drip was leaking Once this as rectified at 2 10 P.M a very satisfactory response to the rfonad was obtained

This flexibility of the blood pressure to suit the rgeon's requirements could not have been obtained th the methonium salts, particularly in a child of t g.

Case 2—A woman, aged 32, underwent for excision of an aneurysm of the middl artery After the aneurysmal sac had been its neck was found to be too broad to clos single tantalum clip. It proved necessary del to divide part of the aneurysmal neck and to afterwards with a second clip When the opened quite a severe hæmorrhage took plac this reason, and to facilitate closing the open the sac, the blood pressure was rapidly lower 36 mm Hg for two minutes (A on fig 2) Afte closure was effected, and before the dura mat closed the systolic blood pressure was restor 90 mm Hg to arrest all bleeding points This elev of the systolic blood pressure from 36 mm to 90 m was effected in ten minutes after stopping the a drip and reducing the tilt of the table to about 15

Case 3—A woman, aged 47 was admitted o morning after an intracerebral hæmorrhage th before This was the fourth subarachnoid hæm the past three weeks She was thought to be b the day of operation

At *operation* which was the day of a bleeding site being an intracerebral clot was fo origin of the right middle cerebral arter impossible to dissect this out, so four clips were on the wall of the aneurysm to obliterate it To this possible it was essential to keep the blood pre low in case of hæmorrhage The systolic blood-pre was maintained between 56 mm and 70 mm for this stage of the operation by running the a drip in a continuous stream, and was main by increasing the tilt of the table to 35°–40 Trendelenburg, as well as by giving 500 mg of

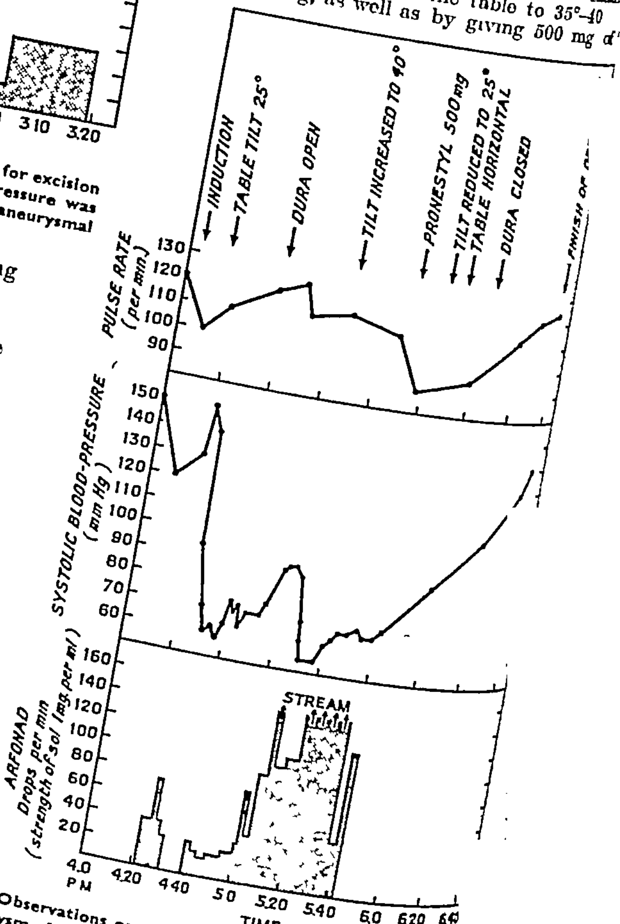

Fig 3—Observations on a woman aged 47 undergoing aneurysm of the middle cerebral artery and removal of The blood pressure was kept low with arfonad supplemen pronestyl while four clips were being placed on the wall aneurysm to obliterate it.

styl to enhance the effect of the arfonad (fig 3) Altogether
patient received 600 mg of arfonad Her systolic blood
sure returned from 70 mm. to 90 mm Hg eighteen
utes after the drip was stopped and was back to her
nal level of 140 mm. by the end of the operation, forty
utes later

his patient was large and healthy and it would have
ved very difficult, if not impossible to produce these
ible results with methonium salts

Conclusions

or operations on the cerebral blood vessels hypo
sion is essential For this purpose arfonad is
erior to the methonium compounds for, being short
ing it gives the anæsthetist greater control of the
d pressure but still reduces the hæmorrhage and
acranial tension to the satisfaction of the surgeon
lowever, it must be emphasised that arfonad is no
wer to the dangers of hypotension, and should only
used in selected cases where the risk is necessary to
uce the greater risk of the operation

Summary

he results are reported of a trial of the hypotensive
nt arfonad in 52 major craniotomies.

he advantages of arfonad over methonium com
nds are discussed

he particular value of arfonad in the vascular surgery
the brain is emphasised Records of 3 cases made
ing operation are illustrated

ll these craniotomies were done by one of us (W McK)
anæsthetists were Dr Donald Blatchley Dr David
rman, Dr Sheila Anderson and Dr Edith de Winter of
neurosurgical unit St. George's Hospital, and Dr Aserman
Dr Cyril Sanger of the National Hospital for Nervous
eases Roche Products Limited kindly supplied the arfonad

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RESULTS OF TREATMENT OF INFANTILE CEREBRAL PALSY

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ON an average 130 cases of motor retardation are
rly referred to the cerebral palsy unit of Queen Mary's
spital. The 200 cases discussed here are now under
atment they were referred at ages between 6 months
d 15 years (average age 6½ years)

Treatment was provided for those with motor dys
nction either in the unit or in the child's home. Where
me treatment was instituted the parents were carefully
tructed in the management of their children through
t the day and progress was checked monthly at our
ebral palsy advice clinic held by courtesy of the
thorities at Lambeth Hospital Cases selected for
patient treatment at Queen Mary's Hospital were
ually of normal intelligence but with grossly disabled
otor systems or poor home facilities or both

Treatment is directed towards attainment of normal
ivity including speech; but traditional methods of
ysiotherapy occupational therapy and speech therapy
not employed, and no traditional apparatus drugs
surgery are used Educational facilities are provided
all children over 3 years of age who are inpatients, and these are as nearly as possible those which are provided in ordinary schools The teachers in the cerebral palsy classes are like the rest of the staff, specially trained in the management of motor-deficient children of this type

"Intelligence testing" of any subject must of necessity be *inferior to the test of intelligence afforded by the whole life situation.* The value of formal tests must depend on the skill of the tester this skill becomes of even greater importance where there is defect of the motor apparatus or of sight or hearing Thus one educational psychologist engaged in research into the educability of the cerebral palsied has given up verbal tests and now bases her evaluation of the intelligence quotient on tests of motor competence (Dunsdon 1952) But this is to exchange one component of the thing to be tested for another Certainly intelligence can only be expressed through the motor mechanism, but if this mechanism is defective tests of its competence will not accurately reflect the intelligence using it and moreover the intelligence quotient will shift with changes in motor performance. We base our estimate of intelligence on the response of the child to the life situation itself (Collis 1953)

In the 200 cases here discussed mostly sent to us with a diagnosis of spasticity and mental retardation our findings have been as follows

A group of 26 were found to have unsteadiness of movement (athetosis) and to be of normal intelligence

"Athetosis" is not properly a diagnostic term: originally it was applied to the symptom which Dorland's *Medical Dictionary* describes as "a constant recurring series of slow vermicular movements" Nowadays it is often used as a diagnostic term to cover many different kinds of cases including cases of abnormal movement in mental defectives unmodified reflexes in spastic patients, variable rigidity and even the unsteadiness of ataxia *Here I am using* "athetosis" only to cover that group of cases in which the *sole* neurological abnormality (apart from occasional deafness) is a distortion of normal movement (which may or may not be "vermicular")

Of these 26 14 are now up to normal standard for their ages and are attending ordinary schools; 7 are up to normal standard for their ages in the cerebral palsy class at Queen Mary's Hospital 4 remained at special schools for handicapped children where they were already established; and 1 attends a school for the deaf and is up to normal for his age

Of the remaining 174 cases, 25 were found to be cases of variable rigidity and mental deficiency and these 25 children attend special schools for backward children or remain at home. There were 3 cases of ataxia and one of these attends a school for the deaf where he is up to normal standard while the other 2 are mentally subnormal and are taught at home

The remaining 146 were cases of spasticity and 6 of them are still inpatients in the unit. Of these 6, 2 are of normal intelligence and attend the cerebral palsy class, 2 who are mentally subnormal also attend this class and 2 are not yet of school age Among the outpatients 8 attend *normal schools,* and 132 (including 10 hemi plegics) attend special schools or have home tuition; all these are mentally subnormal in greater or lesser degree

This gives an estimate of normal intelligence in only 20% of cases referred and this 20% includes all those with athetosis (26) 13 with spasticity and 1 with ataxia Of the remainder (mentally subnormal) 67% had spasticity 12% had variable rigidity and 1% had ataxia

In cases of infantile cerebral palsy a classical clinical picture is expected to develop but our 12 year study has shown that the appearance or non appearance of classical neurological signs deformity and motor dysfunction largely depends upon the physical handling the children receive in the early stages. It has been found that where intelligence is normal the young child can learn to use his defective motor system in a *normal manner* and deformity does not develop It has also been found that even where gross dysfunction and deformity are already established, the condition of affected children can be greatly ameliorated, and those of normal intelligence become able to express their mental processes intelligibly in movement, including speech Those of subnormal intelligence, though their achievements are limited by their mental incapacity, become efficient in greater or lesser degree and often cease to be a grave burden to their families

I am grateful to Dr C D S Agassiz for permission to publish data obtained at his hospital, Queen Mary's Hospital for Children

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EFFECTS OF INHALATION OF SULPHUR DIOXIDE BY MAN

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In the London fog of December, 1952, the densest concentrations of sulphur dioxide were 1 339 p p m and of smoke 4 46 mg per c m on Dec 7 and 8, when the fog was at its worst (Scott 1953, Logan 1953) Both values are much greater than normal for that season of the year In this connection the results of our laboratory studies of the respiratory response of man to low concentrations of sulphur dioxide are of interest

METHODS

Concentrations of sulphur dioxide were established in a 2 c ft 'Lucite' chamber by metering in diluted sulphur dioxide (1% in air) from a steel cylinder The sulphur dioxide joined the main air-stream (5 c ft a minute) before entering the chamber so that mixing was achieved The concentrations of sulphur dioxide in the chamber were measured by the conductivity method of Thomas and Abersold (1929)

The subjects of the experiment were at breathed through a face-mask A slide valve hid their view enabled the mask to be connected chamber without their knowing it The vol expired air was measured in a spirometer, whic read every minute The respiratory rate and p were obtained with a pneumotachograph (Silverman Whittenberger 1949), a device for instantaneous recor of air flow during breathing It consists of a fine 'M wire screen mounted in a face mask The screen mea the movement of air by measuring its velocity volume through the screen by pressure loss or resist of the screen, which bears a linear relation to the The pressure corresponding to the flow is measured a thin membrane whose movement is transmitted electrical recording device From the direct trac whole breathing pattern, inspiratory and flow-rates, and other breathing characteristics obtained

RESULTS

The ability to detect sulphur dioxide varied from person to person Concentrations of 1-2 p were not usually detected At 5 p p m most complained of a slight feeling of dryness in the and upper respiratory passages, but they could actually "smell" it One person found 5 p p m objectionable that the exposure was stopped after minutes, whereas others barely noticed it. Pe exposed to 6–8 p p m definitely detected dioxide in the air but said they became accusto it as the exposure continued

Fourteen normal people exposed to sulphur 1–8 p p m showed changes in respiration and p Tidal volume decreased, respiratory rate incr minute volume remained unchanged, and puls increased

Fig 1 shows the average values of tidal respiration-rate, and pulse rate for five people ex for ten minutes to 5 p p m The same pattern of c was followed by each person Tidal volume fell sh at first and then levelled off at about 25% below control value Respiration increased by three or breaths a minute, and pulse rate by eight or nine the control levels when exposure ceased These values all return

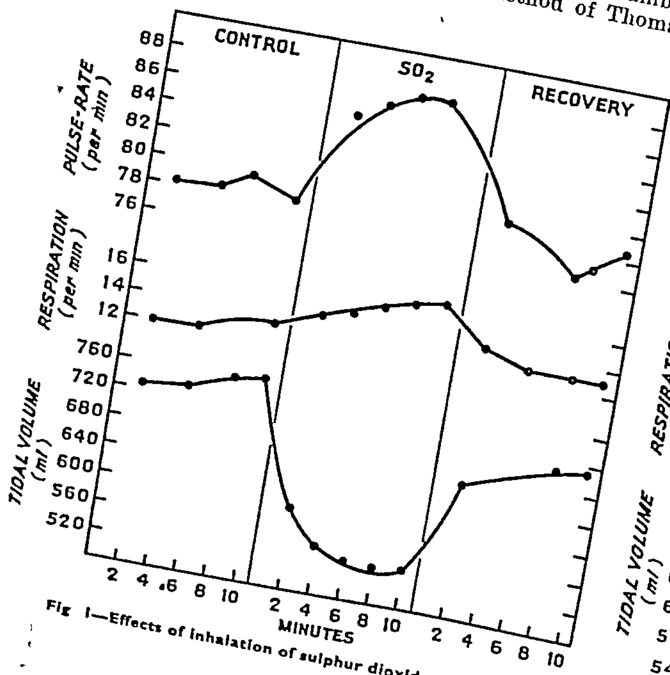


Fig 1—Effects of inhalation of sulphur dioxide 5 p p m

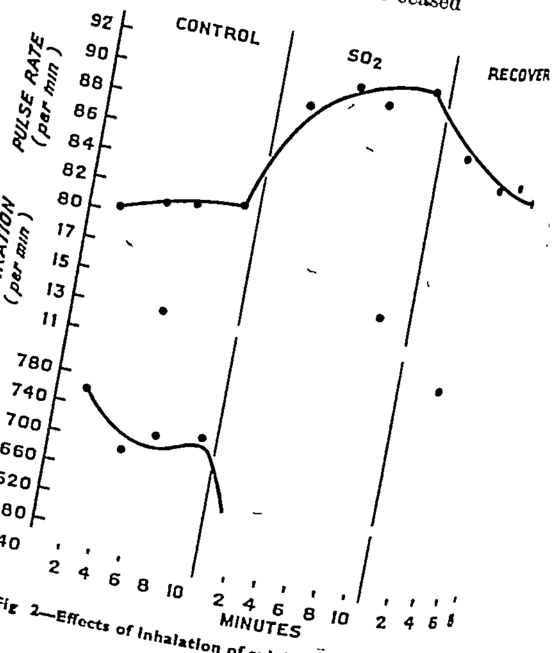
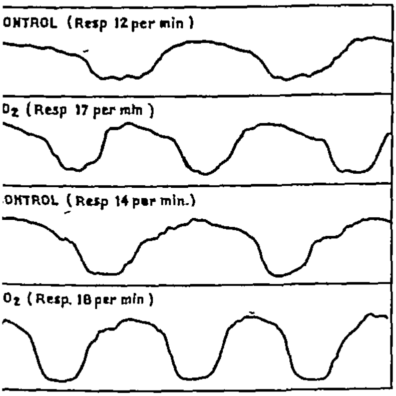


Fig 2—Effects of inhalation of sulphur dioxide 1 p.p.m.

2 presents the average of four people exposed to m It is at once plain that the pattern of changes he same as that for 5 p p m The tidal volume ased during the first two minutes' exposure to about below the control levels During the remainder of posure period however it increased again to about below control values

3 shows respiratory tracings obtained from two e one exposed to 2 p p m and the other to 1 p p m. ncreased respiratory rate is indicated The area the curves may be taken as an indication of tidal ne although this method was not used to measure it. e people so far discussed had no routine exposure lphur dioxide To determine whether the same s would be obtained from people regularly breathing spheres containing sulphur dioxide two men from dustrial plant were exposed to 5 p p m These men d tending boilers in which an oil of high sulphur nt was burned. The concentrations of sulphur le in their working environment often exceed the



—Pneumotachograph tracings. Upper portion of tracing is expiration, lower portion is inspiration.

ican maximal allowable concentration of 10 p p m ded for eight hour exposures (*Archives of Industrial ene and Occupational Medicine* 1952) Fig 4 shows esults of the tests on these two men Apart from a ble transitory increase in respiration the changes ved in the other people were not shown by these

This seems to show that respiratory and cardiac nses to sulphur dioxide were less in them than in le who had not previously been exposed to it gard (1923) states that the apparent tolerance of men is due to chronic inflammation of the upper assages producing a tenacious mucus which acts as otective coating In his opinion deadening of the k has removed one measure of protection

DISCUSSION

lphur dioxide in concentrations as low as 1 p p m produce shallow rapid respiration and increased e-rate. We have previously shown (Amdur et al) that comparable respiratory changes are produced sulphuric-acid mist in concentrations as low as mg per c m Although we have seen no report of entrations of sulphuric-acid mist during the peak e London fog this substance is a known constituent ch fogs

l the subjects of our experiments were healthy men 28–58 No persons with pre-existing respiratory or iac disease were studied.

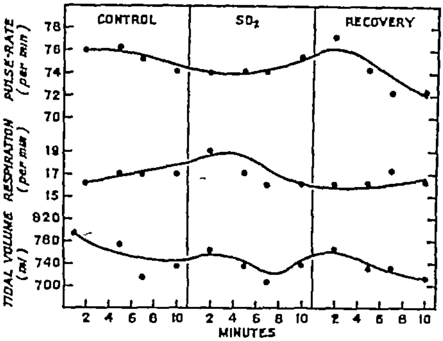


Fig 4—Effects of inhalation of sulphur dioxide 5 p.p.m by workmen (A and B) regularly exposed to high concentrations of this gas.

SUMMARY

Normal people inhaled sulphur dioxide 1–8 p p.m through a face mask for ten minute periods

In all of them shallower and more rapid respiration and increased pulse rate were observed during exposure Similar but slighter changes were observed with sulphur dioxide 1 p p m

Men who worked daily in atmospheres containing sulphur dioxide 10 or more p p m showed no changes when exposed to 5 p p m

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POLYCYTHÆMIA WITH FIBROIDS

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The following case is recorded because manifest and serious polycythæmia disappeared immediately after removal of large uterine fibroids by hysterectomy together with bilateral salpingo-oophorectomy

CASE RECORD

A married woman aged 48 was referred to the outpatient department on Feb 14 1951 with two years history of attacks of transient blurring of vision soreness of the eyes and muscular fatigue. She had always been of high colour but this had noticeably increased during the previous two years She denied headache or dyspnœa No history of drug treatment or exposure to chemical agents was obtained. Menstruation had been irregular for two years with scanty loss, and at no time had she had menorrhagia. Her previous health had been good, and there was no relevant family history

On examination she was small (weight 100 lb) with congested face and bloodshot eyes Her whole skin was deep reddish blue Her retinæ were deeply coloured and the retinal veins engorged. Her abdomen contained a large mass rising from the pelvis and extending upwards to the umbilicus A further mass, freely mobile and as big as an orange, was present in the left hypochondrium There was no enlargement of the liver or of the spleen The cardiovascular system appeared normal, the blood pressure was 160/90 mm Hg No abnormal signs were found in the respiratory and central nervous systems There was no finger clubbing The urine contained neither albumin nor sugar

Investigations—A blood count showed red cells 7,280,000 per c mm, Hb 148%, colour-index 1 0, white cells 5800 per c mm (polymorphs 78 5%, eosinophils 1 5% lymphocytes 15%, monocytes 5%), platelets 125,000 per c mm, packed cell volume 72 c cm, mean corpuscular volume 88 c μ, mean corpuscular hæmoglobin concentration 30%, bleeding time 1½ minutes, clotting time, initial 6½ minutes, final 7 minutes, prothrombin time 18 5 sec with control 25 sec The plasma volume was 2040 ml (Evans blue method)—i e, the blood volume was 7286 c cm Radiography of the chest showed lungs striated, but no other chest abnormality" No evidence of arteriovenous aneurysm was found on screening the chest The long bones were radiologically normal These results excluded polycythæmia vera but did not reveal any of the recognised causes of secondary polycythæmia

Operation—Laparotomy was done by Prof Hugh C McLaren on March 27, 1951, and the abdominal masses were found to be multiple fibroids, one of which was pedunculated and freely mobile Total hysterectomy, bilateral salpingo oöphorectomy, and appendicectomy were done without untoward incident or excessive hæmorrhage The spleen was not enlarged

Postoperatively the patient's recovery was uneventful Pathological examination confirmed the nature of the tumours

Date	Red cells per c mm	Hb %	Colour index	White cells per c mm	Platelets per c.mm.
Jan 24 1951*	7,640 000	140	0 92	6700	
Feb 14 1951	7 770,000	148	0 90	6600	101,000
March 2 1951	7,430,000	148	1 00	6100	159 000
March 5 1951	7 280 000	148	1 00	5800	125,000
March 27 1951			Laparotomy		
April 3, 1951	5,680,000	114	1 02		
April 9 1951	5,580 000	117	1 01		
April 11 1951	5,620 000	110	0 98		
May 23, 1951	6 110 000	112	0 93		
July 25 1951	4 190,000	84	1 00		
Sept 27, 1951	5 020 000	100	1 00	5000	258 000
Nov 21, 1951	4 600,000	92	1 00	6500	
Jan 30 1952	4,840 000	94	0 97	6400	218,000
July 16, 1952	5,110,000	102	1 00	5700	
Jan 21 1953	4,750,000	92	0 97	7700	238,000

* This count was made at All Saints Hospital, Bromsgrove, W

A week after operation the hæmoglobin value had fall 114%, and it continued to fall to normal levels blood counts have shown no recurrence of poly during the last twenty-two months (see table) The symptoms have been completely relieved.

COMMENTS

We have been unable to find any published rep an association of secondary polycythæmia with fibroids, nor any record of its complete relief by removal of the tumours We can suggest no explanation of this phenomenon

Medical Societies

ASSOCIATION OF CLINICAL PATHOLOGISTS

THIS society met in London on Oct 1–3 Dr E N DAVEY (Gloucester) was appointed president elect The chairmen at the various sessions were Prof Matthew Stewart, Colonel L R S Macfarlane, Prof R Knox, Dr J V Dacie, Prof J Heimbeck (Oslo), Prof R J V Pulvertaft, Mr C P Stewart, D SC, and Dr H B May

Nævi and Malignant Melanomas

SOPHIE SPITZ and ARTHUR C ALLEN (New York) discussed the clinicopathological correlation of nævi and malignant melanomas Their many beautiful illustrations were chosen to show how difficult it may be to confirm or exclude malignancy in pigmented tumours After presenting their classification and describing the various clinical and histological types, they reviewed the evidence in support of humoral activation and referred to the receptivity of the newborn to secondaries transmitted from the mother By contrast only two instances of primary melanocarcinoma had been recorded in infants, and in neither case was the evidence satisfactory

GEORGIANA BONSER (Leeds), who opened the discussion, referred to the part played by trauma in causing malignant transformation Dr ALLEN believed that it was very commonly held that trauma of a nævus was fraught with danger, but that in practice it was the junctional nævi which were liable to undergo malignant change and these were the ones most commonly found on many of the areas liable to trauma such as the sole of the foot Perhaps therefore the so called vulnerable areas were vulnerable because junctional nævi were so commonly found there

Professor STEWART referred to an instance in which the malignant cells had evidently been kept in subjection for a long time A large necrotic mass had been found in the sacrum but at necropsy metastatic melanocarcinoma was found in the liver It transpired that an eye had been removed some years earlier on account of a malignant melanoma the pelvic mass was deemed to be a greatly delayed secondary while the liver deposits were assumed to be tertiaries

Malignant Hypertension

G J CUNNINGHAM (St Bartholomew's Hospital) described two cases of malignant hypertension with kidneys which were partly smooth and partly granular The first was a 60 year old with mild hypertension whose illness suddenly became more acute and serious 3 years later She presented on second occasion with dyspnœa, vomiting, and bot and visual disturbances The blood pressure was mm Hg and the blood urea 352 mg per 100 ml De followed The second patient was a man, aged 30 w intermittent claudication 5 years later he suffered paroxysmal dyspnœa with a blood pressure of 270/1 Hg He died soon afterwards in coma Each case w to have aberrant renal arteries, one of which had le obstructed by a thrombus It was a matter of interest the parts of the kidneys supplied by the thrombosed showed mild hypertensive arteriosclerosis—the smooth —while the remainder of the kidneys supplied by the p vessels were grossly diseased, containing numerous an fibrinoid degeneration in both glomeruli and arterioles aberrant vessels were normal in appearance but the bosed vessels revealed underlying atheroma of a degree sufficient to produce a measure of obstruction and to the development of severe lesions in those parts organ Because of the resemblance of the kidneys to produced experimentally by Byrom and Wilson in Dr Cunningham referred to his cases as "a nat occurring experiment"

Colitis Cystica Profunda

H B GOODALL (Dundee) described two examples of c cystica profunda The first patient had suffered from cytic anæmia and mucous diarrhœa followed by pe obstruction the second from chronic ulcerative colitis severe bleeding In neither case were pathogenic org found The peculiar breaches in the muscularis m secondary to abscess formation, were believed to be of cance and the probable cause of the ingrowing mucus-sec epithelium and the consequent formation of cysts

Epiloia

L CROME (Fountain Hospital) dealt with the st features of epiloia, and indicated their relative fre Incomplete forms of the disease should be sought parti among the relatives of patients with the fully disease Dr Crome described in his series two fibroelastosis of the heart and referred to two other examples

Malignant Disease of Bone

Professor PULVERTAFT and J G HUMBLE (W Hospital) demonstrated a film prepared by phase- microscopy which included examples of myelomatos other malignant conditions of bone

Epidemic Hæmorrhagic Fever

Colonel **Hugh R. Gilmore** (Washington) described the nical and pathological features of epidemic hæmorrhagic or sometimes called Korean fever Although fighting gan in Korea in June 1950 it was not till the summer of 51 that the disease was recognised in United Nations troops, d it reappeared in 1952. It has affected only troops in the gion of the 38th parallel and in rural areas it has not been ted in Southern Korea. Cases have first appeared in May th the advent of the light spring rains and have reached peak in June The incidence curve then falls after the mmer rains and rises to a second and higher peak with the season in October The incidence of the disease in a litary unit is not heavy for only a few individuals in a mpany may be affected and they may all be in the same uad There has been no evidence of spread from person to rson or through water or food but it has been noted that ldiers may contract the disease after being confined for a ile to certain areas, suggesting therefore an insect vector ited States workers consider a trombiculid mite (chigger) be the responsible vector and these are known to be tributed in highly localised foci at a time when the disease urs and to have a limited range of movement Japanese d Russian workers however earlier believed that the ease was conveyed by *Laelaps jettmari* a mite found on the mmon field mouse. Although there would appear to be re support for the former view the disease has not so far en transmitted to animals, and both the causative agent and means of transmission remain unproven Second attacks ve not occurred.

The onset is acute with a febrile stage accompanied by dache back pain and anorexia Nausea and vomiting are mmon after the first 24–48 hours. The patient may complain photophobia blurring of the vision, and orbital pains, ile a scarlatiniform rash of the face and neck earlier on in disease is typical together with infection of the conjunc- a and pharynx Albuminuria appears about the 3rd or 4th y together with casts and often erythrocytes One should itate to make the diagnosis in the absence of albuminuria ter 3–5 days the fever subsides and convalescence begins the more serious cases, however petechial hæmorrhages pear about the 4th day on the palate and shortly afterwards ng the axillary folds and the lateral chest wall and neck od may appear in the urine stool or vomitus Subcon ctival bleeding was common in the outbreak of 1951 but s frequent in 1952 During the hæmorrhagic phase there y be repeated episodes of shock during which the patient y die The shock is accompanied by oliguria, azotæmia, d persistent vomiting but if recovery occurs a period of uresis follows. The mortality rate was 8% in 1951 and about in 1952

Leucopenia is usual in the early stage but later there is cocytosis with an increase of immature granulocytes. out 90% of patients show an increased capillary fragility the Rumpel Leede test while moderate thrombocytopenia urs in about 75% of the patients The shock which appears be responsible for about two thirds of the deaths is umed to be due to loss of serum through damaged illaries Deaths in the later phases are associated with hydration fluid and electrolyte imbalances and renal lure Necropsy findings include hæmorrhages in the kidneys, ht auricle anterior pituitary and occasionally the adrenal cal hæmorrhages have been seen in the meninges and in Focal myocarditis and mild diffuse interstitial pancrea is have been observed in some cases while there may be rosis of the anterior lobe of the pituitary extending into infundibulum of the pyramids of the kidney of the renals and occasionally of the islands of Langerhans The ions suggest the presence of an agent which causes capillary mage and either directly or on account of tissue anoxia, lular necrosis There is no swelling of the capillary endo lium as in typhus. No treatment has been found to be of all other than absolute rest Evacuation by helicopter her than by ambulance is believed to have saved lives. te-repellants are now freely and successfully used in the ected areas.

Intestinal Spirochætosis

A. G. Sierra (Eastbourne) described instances of intestinal rochætosis associated with persistent relapsing diarrhœa.

Staphylococcal Coagulase

E. S. Duthie (Southampton) spoke on the mode of action staphylococcal coagulase which is of two sorts—the bound and the free The former acts directly on the fibrinogen of certain animals and is the one concerned in the slide test commonly employed; the latter which is responsible for the reaction in the tube test is liberated in the culture medium and clots any fibrinogen provided that an activator is present. Bound coagulase is liberated in autolysis and its presence can be shown by an antibody inhibition test. Reference was made to the value of these separate forms of coagulase in the preparation of vaccines

Laboratory Investigation of Poliomyelitis

G. L. Le Bouvier (Colindale) described recent developments in the laboratory investigation of poliomyelitis, mentioning in particular the value of tissue culture in the identification of the strains of the virus. Type 1 was first identified in this country in London in June 1946 type 2 in Stowmarket in August 1951 and type 3 in Cardiff in December 1951 All three types occur from time to time. The complement fixation test is held to be of little worth in the diagnosis of the disease, but it is of value in epidemiological studies.

Hæmophilia and Christmas Disease

J. R. O'Brien (Plymouth) discussed the differential diagnosis of hæmophilia and Christmas disease for several families credited with having had the former are now known to have had the latter Patients with Christmas disease have a long, although sometimes a normal, clotting time an abnormal prothrombin consumption, and a delay in thrombin generation In the laboratory the defect can be made good by normal plasma The thromboplastin generation test is used to decide whether the fault lies with the serum factors amongst which is the Christmas factor or the alumina-treated plasma fraction containing the antihæmophilic globulin Blood used in transfusing these patients must therefore contain the Christmas factor the anti hæmophilic factor being unnecessary In a patient studied over a period of 5 months it was noted that the clotting and prothrombin-consumption times were readily restored to normal with blood and plasma transfusion but that 4 pints was usually needed to restore temporarily the thromboplastin generation test to normal and bring about a cessation of the bleeding

Erythræmic Myelosis

G. Discombe and **K. H. Nickol** (Central Middlesex Hospital) described a case of erythroleukæmia in which the prolongation of life by means of transfusion had made it possible to study the pathological process at a later stage of the disease The patient a man aged 72 eventually developed an acute granulocytic leukæmia and died of cerebral hæmorrhage These workers suggest that as nothing is known as to their pathogenesis the so called erythræmic myelosis or Di Guglielmo's disease and acute leukæmia with erythroblastic onset should be grouped together

Sickle cell Trait

H. Lehmann (St Bartholomew's Hospital) dealt with the distribution of the sickle-cell trait In negroid Africa the highest incidences are found in the north and east falling somewhat towards the west and diminishing towards the south, so that in South Africa it is virtually absent In Uganda it is about 20% in the Nilotic-speaking tribes but almost nil in those speaking a language related to Hamitic. In the Bantus the incidence of the trait varies in inverse proportion to the degree to which they were in contact with the recent Hamitic invaders. Thus it might seem that the trait came from Asia In Europe some sickle-cell trait carriers are found in Italy and a few isolated pockets with high incidence exist in Greece Wherever the sickle-cell trait is frequent there is malaria, a low social status and close inbreeding

Diagnosis of Myelomatosis

J. G. Humble and **V. F. Maclagan** (Westminster Hospital) discussed sternal marrow findings and flocculation tests in the diagnosis of myelomatosis.

Iron containing Granules in Erythrocytes

A. S. Douglas and **J. V. Dacie** (Postgraduate Medical School of London) described the incidence and significance of iron-containing granules in human erythrocytes These were found to be present in reticulocytes but rarely in adult erythrocytes except following splenectomy They believed that the spleen might be responsible for the assimilation of iron in the synthesis of the hæm molecule

Tests in Burned Patients

S SEVITT (Birmingham) had made use of corticotrophin (A C T H) or adrenaline to determine whether acute adreno cortical failure in burned patients was still present after the eosinophils had returned to normal Of 14 patients tested with corticotrophin 12 gave normal eosinophil depression curves indicating normal stimulable reserves of the adrenal cortex The remaining 2 failed to produce eosinopenia The 1st ultimately died, but a few days after the test spontaneous eosinopenia developed, indicating that if failure had occurred earlier it was of short duration The 2nd patient continued to produce abnormal curves until the 16th day when the test became normal In 9 of the 12 patients tested with adrenaline normal curves were found Abnormal results were found in 2 children who had become confused and irrational Since adrenaline produces eosinopenia indirectly, probably via the hypothalamus, its lack of eosinophilic effect in a patient reacting normally to corticotrophin is probably due to pituitary or hypothalamic disturbance

Test for Tuberculous Meningitis

The value of a test for early tuberculous meningitis based on the passage of bromide from the blood to the cerebrospinal fluid was reported by HONOR SMITH and G HUNTER (Oxford) The transference of this substance appears to be greatly facilitated in tuberculous meningitis when compared with comparable forms of meningeal inflammation

Demonstrations and Address

The next session was devoted to demonstrations and to r R G MACFARLANE's film on sternal puncture There ter Prof DOROTHY RUSSELL delivered a presidential address rinted on p 771)

Tests of Pituitary Function

J HARKNESS and C DONOVAN (Portsmouth) had confirmed the findings of Stewart, Horn, and Robson (1953) in which it was shown that corticotrophin causes an increase in the plasma total ascorbic acid together with an increased proportion of ‘ reduced ascorbic acid,” whereas cortisone causes no change in the total level although there is an increase of ‘reduced ascorbic acid ” They now described a test of pituitary function based on the ascorbic acid levels after an injection of corticotrophin The degree of response in some psychotics was found to be lower than in normal controls Changes similar to those produced by corticotrophin were noted after electroconvulsive therapy, emotional stress, oral sodium salicylate, or phenyl butazone

Steroids and Water Metabolism

M LAMOTTE and L JUSTIN BESANÇON (Paris), whose paper was presented by J J BERNIER, referred to the influence of steroids on water metabolism Œstradiol was effective in increasing the total water content of the body but glomerular filtration remained practically unaltered although the calculated renal plasma flow was slightly lessened Diuresis provoked by water consumption was not modified, but when brought on by saline it was considerably lessened Sodium chloride was not eliminated, the arrest of the sodium being the reason for this Testosterone, on the other hand, induced an increase of weight without any increase of either total or extracellular water in other words the increase of weight was due to an increase in body tissue The renal plasma flow however, was increased as was also the diuresis induced by water or saline The elimination of sodium was only impaired if the kidneys had been previously damaged Cortisone caused a marked retention of water and sodium yet increased both glomerular filtration and the renal plasma flow Notwithstanding this diuresis induced by the ingestion of water was increased In these studies the total water-content was estimated by the antipyrin method, and the extracellular water by the mannitol technique

Postoperative Retention of Salt and Water

A V G LEWIS and L P LE QUESNE (Middlesex Hospital) ealt with the problem of the postoperative retention of salt nd water For 24–48 hours after operation (the observations ere made on gastrectomy patients) there is a diminished cretion of water the result of release of antidiuretic hor one This is due to the emotional disturbance associated th the operation and is probably accentuated by morphine and anæsthesia Sodium retention occurs in two phases, separated by an increased sodium excretion the fir the day of operation, is probably mainly due to hæmody factors, the second, usually beginning on the 3rd day, be considerably reduced by ensuring a reasonable potas intake throughout In some cases, particularly wh potassium was given, continuous postoperative sodium water retention could be observed In the discussion w followed reference was made to the value of weighing for the rapid assessment of sodium and water retenti

Fallacies of the Test-meal

F AVERY JONES (Central Middlesex Hospital) refer the fallacies of the test meal The shaded area on many meal charts corresponds to the findings in 80% of Be and Ryle's series of healthy subjects The remaining although they show less or more acid than the majority, nevertheless in perfect health A high or low reading the should not be taken to imply an irregularity of gastric fun Follow up studies on patients with high readings have shown any correlation with dyspepsia, unless there wa increased volume of secretion A high acid curve ma due to rapid emptying or to hypersecretion Achlorhydria clinical practice implies a gastric juice with pH greater 3 5, but at this level there is still a little acid present Pa with histamine fast achlorhydria may be studied furth 24 hour pH curves, those with primary anæmias give a of 4 5 or higher, whereas those with ulcer dyspepsia have acid for many hours throughout the day The main ind for a test-meal is in those patients with vague sym referable to the upper abdomen in whom radiological have been negative In such cases the test might be h in revealing the presence of carcinoma by gross blood ing and an increased difference between the free acidity Acid is found in at least a third of patients carcinoma of the stomach. Dr AVERY JONES always it valuable to know if the blood reported as present fact gross bloodstaining or merely positive for blood chemical tests He believed that very little was to be from the routine use of test meals in cases of peptic ulc

In the discussion which followed he said that he pref the gruel test meal to the alcohol meal because the produced a more physiological form of distension o viscus A nasal tube was easier for the patient and certainly to be preferred when a 24 hour test was indi The tubeless test meal was probably adequate for the gation of cases of pernicious anæmia He agreed that management of the patient during the test should be hands of an experienced and competent sister familiar all the pitfalls in the technique, and that failure to ob this precaution was liable to produce unsatisfactory misleading results

Tests of Glomerular-filtration Rate

J E CRAIK and A P KENNY (Glasgow) reported a series of 63 patients in whom the thiosulphate and clearance tests had been compared The estimation of pl thiosulphate was found to be unsatisfactory, and mor it appeared that thiosulphate was actively excreted by tubules the excretion becoming maximal at p thiosulphate concentrations of 16 mg per 100 ml. estimation of thiosulphate clearance was inadequate measure of glomerular filtration rate These workers adv evidence that in myxœdema tubular reabsorption thiosulphate is inhibited

Estimation of Serum-cholinesterase

B W MEADE (Westminster Hospital) reported that colorimetric determination of serum cholinesterase was s factory for routine use, but that the test had proved of l value in the diagnosis of thyrotoxicosis

Liver-function Tests in Rheumatoid Arthri

P W DARBY (Westminster Hospital) described his in 50 cases of rheumatoid arthritis in which a battery o function tests had been carried out While positive flocc tests which he obtained represented changes in the s proteins which might or might not be due to liver disea results with Mateer's bromsulphthalein test and the estim of urine coproporphyrin as recommended by Sch showed that in rheumatoid arthritis a degree of liver d exists which is significantly greater than that with ill health from other causes

Reviews of Books

posal of the Dead

C J Polson M D Birm F.R.C.P professor of forensic medicine; R P Brittain M.A B SC M B LL.B Glasg senior lecturer in forensic medicine; T K Marshall, M B Leeds, lecturer in forensic medicine University of Leeds. London English Universities Press 1953 Pp 300 21s

To collect in one volume the more important material ncerning the disposal of the dead was a good idea d this book after a historical introduction deals with diate disposal (including death certification and gistration), cremation burial (including funeral rites) humation embalming and funeral direction Admit lly, if the object were an exact and comprehensive position of the law and practice many of these subjects ould require a textbook to themselves; and though e book is full of useful and curious information it ffers in places from lack of detail

Thus the 4 pages on anatomical dissection would be the tter for expansion The distinction is not clearly drawn tween the main sources of supply to schools of anatomy i.e the unclaimed bodies of persons dying in welfare stitutions, and bodies made available by voluntary bequests ere is also confusion between the Anatomy Act which an Act for Regulating Schools of Anatomy and o practice of post-mortem examinations In references sections of the Anatomy Act the number of the 1940 der extending the period before interment is misquoted d a similar Order for Scotland, which preceded that for gland and Wales by twenty four years is not mentioned d a reference to the forms required at Leeds, little is which would help funeral directors to deal with the al procedure in cases where a voluntary bequest has been o for anatomical dissection The chapters on cremation l embalming are excellent but that on international ansport of the dead refers neither to the sailor s dislike of rrying bodies on a ship nor to the International Agreement ncerning the Transport of Bodies signed in Berlin in 1937 though this has only been ratified by some dozen untries

For such reasons it would perhaps be well to make the xt edition rather larger But in its present form it ls the greater part of a considerable gap The medical ader will find much to inform him and so of course ll the funeral director, for whom the book is primarily tended

he Surgery of Infancy and Childhood

Its principles and techniques Robert E Gross, M D D SC., William E Ladd professor of children s surgery Harvard Medical School. Philadelphia and London W B Saunders. 1953 Pp 1000 80s

This is the record of Professor Gross s long experience he subject covered is pædiatric surgery—after the ortho-ædic surgeons have claimed the fractures and deformities, e plastic surgeons the cleft lips and palates the nose and hroat surgeons the glands of the neck and the disorders f the nose and throat and the neurosurgeons the ills of heir chosen domain Professor Gross is fortunate in etaining the chest and urological surgery which in this ountry would also probably go elsewhere However here is more of the child left than one might suppose nd in each of the 61 chapters of this book there is a orking plan for the diagnosis, treatment, operation and ftercare of a disability The author has himself tried nd proved the steps recommended and the young urgeon who has had little experience of children s urgery could follow the instructions and never go far rong. It is a book which could never be written by young man: not a word is based on hearsay or heorising

Certain differences in approach and technique from ours re inevitable Few anæsthetists in large centres in England, or instance would nowadays agree that the open mask drop method is the anæsthesia of choice for these cases though hey would have done so ten years ago Drainage is advocated or appendicitis with peritonitis more often than would be the case here Infants with hypertrophic pyloric stenosis are given 10% glucose intravenously 10 ml per lb per day and subcutaneous saline 15 ml per lb per day The 10% glucose is hypertonic and makes adults very thirsty and the amount of subcutaneous saline administered is equivalent to giving 10½ st man 2250 ml of fluid subcutaneously every [illegible] four hours—an experience from which even the stout [illegible] would shrink.

Discussing duodenal atresia Professor Gross [illegible] of careful assessment of the child s mental state [illegible] made since many children with duodenal a[illegible] mongols—the implication being apparently t[illegible] thought to be mongols should be allowed to [illegible] seems dangerous reasoning But if his book [illegible] evokes opposite opinions it is nevertheless [illegible] deserves to find an honoured place in all pæd[illegible] centres.

Stress and Disease

Harold G Wolff M.D professor of medicine [illegible] logy) Cornell University Springfield Ill Ch[illegible] Thomas. Oxford Blackwell Scientific Publ[illegible] 1953 Pp 199 40s

This monograph in the American Lectures in [illegible] logy series brings together in a small volume [illegible] original work which Professor Wolff and his col[illegible] have already published It offers a concise re[illegible] some of man s reactions to danger and his a[illegible] responses which Dr Wolff has done so much to [illegible] by controlled experiment Many of his results a[illegible] known, for he is a pioneer of the scientific inves[illegible] of the effects of emotion on the human body To [illegible] the concepts expounded may seem too wide and comprehensive, the arguments uncritical; to [illegible] the evidence will be convincing But none can fail [illegible] fascinated by the skill and brilliance of the w[illegible] Broad principles are related to particular exampl[illegible] demonstrable changes in the subject These are [illegible] based on animal studies but on the results of [illegible] stimuli to the skin the stomach, the colon, the [illegible] or other organs of the human being Many [illegible] conclusions seem common-sense comments on [illegible] observations but it is rare to find them so [illegible] expounded Man s reaction to man may be [illegible] as important as his reaction to a microbe and the [illegible] of a danger may call forth responses little di[illegible] from the assault itself Professor Wolff pr[illegible] evidence that man must pay some price for the [illegible] which he lives—and that some of the price of adap[illegible] and reaction may be pain and disease In the cont[illegible] and well adjusted subject the response to an [illegible] or a stress may be transient and harmless but [illegible] conditions of anxiety or resentment, caused by a [illegible] a drug or the mere effort of coping with day [illegible] burdens this same person may react quite diffe[illegible] It is therefore in fostering the adaptive-pro[illegible] response and in changing the way in which a par[illegible] subject perceives a stress that the physician m[illegible] able to do most good; and Dr Wolff believes that [illegible] 730 subjects two out of three were constructively a[illegible] during a three year period of study The main ther[illegible] peutic aim was to produce tranquillity and freedom fro[illegible] sustained hostility and resentment

Founders of Neurology

Editor: Webb Haymaker, M.D., chief neuropathology section Armed Forces Institute of Pathology Washington D C., with the biographical and editorial assistance of Karl A Baer. Springfield, Ill Charles C Thomas. Oxford: Blackwell Scientific Publications 1953 Pp 47[illegible] 75s 6d

If the purpose of biography is to inspire by examp[illegible] Dr Webb Haymaker and his associates may well [illegible] content with this interesting illustrated collection [illegible] character studies prepared for the Fourth Internatio[illegible] Congress of Neurology To provide in a single vo[illegible] succinct accounts of 133 of the masters of neurology, written by their admirers and in some instances th[illegible] pupils is an achievement of note

It is salutary to be reminded of the prodigious output [illegible] work of Ramon y Cajal of J E. Purkinje (who had to wa[illegible]

years (for his long wanted microscope), and of the versatile Heinrich Obersteiner We read of the stoicism of the youthful Nicholas Achucarro, a victim of Hodgkin's disease, and of Alfons Maria Jakob, a tremendous worker, who suffered for his last 7 years from osteomyelitis and died at the age of 47, and of
teste rseverance of August Forel, who, when most men
sion have surrendered to fate, learned after a stroke to
adrer ft handed, and continued at work for another 19 years
The } Bonin portrays well the polite and genial Rudolph
taneou on Kölliker, who retired from his chair at Würzburg
occurrec) of 85 after publishing twenty papers in his last
continu office Tribute is paid, too, to the memory of
when th alter Campbell, who, fired by the encouragement
with adi gton, did his important pioneer work on
were fo opography in the lonely laboratory of Rainhill
irra
pro cess has come to neurologists for different reasons
in ot and others lived in the heroic age of neurology,
due io made full use of the unparalleled facilities of the
rière at a time when the paralysed were in need of
classification The important contribution of George
Huntington was made in general practice The
Th of Alois Alzheimer, who died at the age of 51, lay in
the pt that he combined the clinical and pathological
fluid h to brain disease Dr A T Rasmussen describes
The efatigable Franz Nissl as "a gnome of a man," a
facilit nd a practical joker, and the portrait of the versatile
comp eir Mitchell, influenced throughout life by Claude
d and also by his vivid memories of the battle of
burg, is ably drawn by Dr Haymaker

Th sidering that these biographies conform to a single
Dr rn, they are remarkably good emphasis has
afte y been laid throughout on an accurate study of
(pri man's character rather than on the bald facts of
urriculum vita Some of the essays are too short
io full justice to their subjects, but the editor, by
ing into the text a running history of neurology,
th done what he set out to do in a most engrossing
it nor
pla
propo

causes

choses passionelles

increa JOREL, Médecin Chef des Hôpitaux Psychiatriques
test ons Expansion Scientifique Française 1952 Pp 472
after 2000

in so ppreciate this book fully one needs to be well
cont inted with classical French psychiatry, and with
trop al French literature Dr Borel draws his quota-
stres from La Bruyère or Molière almost as often as
Lasègue, Magnan, or Esquirol The writers,
ver, to whom he turns oftenest are Ribot and
Mlérambault—Ribot who published his *Essai sur*
pap *passions* in 1906, and Clérambault, the brilliant and
of ac clinician who saw in the mechanism of passion
incre creative force giving rise to diverse psychoses,
iltr *ures passionels* He writes in clear and sometimes
latedr nt language of the physical and psychological
prov teristics of passion and of its pathological forms,
brou he discerns in hypochondria and in mystical
chlo as well as in jealousy, revenge, and erotomania
the inical analyses are careful studies of morbid feeling,
ey owe nothing to psycho analysis, as he points out,
a have more in common with Balzac than with
gache Even those who dissent strongly from his
thod and views will enjoy his lucid exposition and
ively critique

Chemical Physiology of Contraction in Body and Heart Muscle

A SZENT GYÖRGYI, PH D, Institute for Muscle Research, Marine Biological Laboratory, Woods Hole, Mass New York Academic Press 1953 Pp 135 $4 80

THIS book is divided into sections (1) introductory
es on the histology and physiology of muscle, (2) the
d lecular mechanism of motion in voluntary muscle,
a study of heart muscle, and (4) some general views about the factors essential to muscle activity Dr Szent-Györgyi, whose outstanding record in biochemical discovery and thought is well known in this country, here stat [illegible] d amplifies many of the almost revolutionar [illegible] on muscular contraction which caused so much discussion when he put them forward in his earlie book, *The Chemistry of Muscular Contraction*

This new book, he says, "is not offered as a comprehensi and objective review, it is the presentation of a problem as he sees it after fourteen years' experiments with muscl He has "endeavoured to talk in a language understandab to the average biologist, stressing outlines more than detai and hoping to be excused by those who prefer a more technic treatment" In these aims he is entirely successful, for he ha written a stimulating and controversial little book easi to be understood by anyone even slightly acquainted wi muscle physiology and biochemistry His rather quai English is here a great advantage, for he eschews pompo and complicated sentences and produces an effect of clarit and charm

The reader will find here the experimental evidence f the conception of actomyosin (the contractile prote element) made up of actin and myosin, of the "mero myosins" of which the latter is composed, and of the part perhaps played by adenosine triphosphate (A.T.P in the contraction process Here is a fascinating stor about the recent work of his school on heart muscle, and exciting hypotheses about the way in which the nervo impulse may act For all who value inspired speculati and who wish to keep abreast of present-day develop ments in muscle biochemistry, physiology, and patholog this book is indispensable

Thinking

An Introduction to its Experimental Psychology GEORG HUMPHREY, professor of psychology in the Universit of Oxford London Methuen 1951 Pp 331 21s

Professor Humphrey, who in 1933 provided us with a thoughtful book on learning, has now written a learne book on thinking This scholarly work covers a wide an fundamental field of psychology, in which it is easy t miss the wood for the trees but Professor Humphrey mastery grasp keeps the material in such proportio that the reader has the main problem always before hi The first chapter deals with association, and argues th the conditioned reflex theory is the modern form of th classical theory of association, against which muc subsequent experimental work was "an unsuccessfu revolt" This is illustrated by the monumental studie of the Würzburg school, to which the next three chapte are devoted The *Gestalt* theory, and the connectio between thought and motor reaction, are next examined A particularly valuable chapter is devoted to languag and thought, a fuller treatment of aphasia would ha have been welcome, but throughout the book the autho has deliberately abstained from examining patholog thinking, except incidentally and briefly The reade concerned with anomalies such as schizophrenic thinki will therefore find no direct reference to them, but a ri supply of theoretical and experimental data many of which throw light on his problems

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Carbohydrate Metabolism (2nd ed Chicago Universit Press London Cambridge University Press 1952 Pp 336 64s)—This revised and slightly enlarged edition of the well known work by Dr Samuel Soskin and Dr Rachmi Levine will be as well received as its predecessor The authors describe it as a correlative text which brin together biochemical, physiological, and medical knowledg of carbohydrate metabolism in a unique way The claim is substantiated, yet the work remains personal in its presenta tion, stressing, as it does, the authors' particular viewpoints Thus great prominence is given to the rôle of the liver in the control of the blood sugar Besides containing a additional 230 selected references, this edition includes ne material on the interconvertibility of foodstuffs, isotop studies, and hormones—in particular, insulin and the adren steroids As in the first edition there is a good critic account of the significance of *respiratory* quotients, dextrose nitrogen ratios and an excellent review of th mechanisms concerned in ketosis The possible rôle pancreatic hyperglycæmic factor in the apparent action of insulin on liver glycogen has been disregarded, and th discussion of insulin resistance in infections omits any to the adrenal cortex These, however, are small criticisms of a work which will be widely used and appreciated.

THE LANCET

LONDON SATURDAY OCT 10 1953

Our Natural Element

Last year over 4000 people in Greater London lost eir lives in a major disaster This was the fog which escended on the capital on Dec 5 and did not lift ntil Dec 9 No other recorded fog has achieved any ing like this death rate the "smog" in the Meuse alley in 1930 was responsible for only 64 deaths and at in Donora Pennsylvania in 1948, for 20 The creased mortality from the London fog was spread ver the two succeeding weeks and was particularly gh among those aged 45 and over though young ildren too were seriously affected The National moke Abatement Society are as anxious as the rest us that such disasters should not recur, and they pened their twentieth annual conference held at lasgow, from Sept 30 to Oct 2 by discussing how prevent them.

We manufacture our own fogs—wrapping our cities n John Evelyn's classic phrase) in a 'hellish and small cloud of seacoale', but the weather has to ollaborate Under ordinary conditions as Mr A arker D.Sc explained the upper air is cooler than e air near the earth's surface and as the warm air ses there is a constant circulation which produces a reeze or wind Occasionally however the tempera ure at ground level falls below that of the layers ove, which means that no air rises, there is no wind nd if the air is humid fine drops of moisture condense the lower stagnant levels causing a mist or fog In nsely populous and industrial areas sulphur dioxide s and other products of fuel combustion which are rmally dispersed and diluted by the wind collect the stagnant layers in increasing concentration and ve the fog that objectionable flavour and irritating ality so characteristic of the 'London particular

December last year opened with frost and local fogs, llowed by milder weather on Dec 3; then on Dec 4 large anticyclone reached us and stayed until Dec. 8 using frost and fog Milder weather did not reach ndon till Dec 9 The depth of the fog was variable ing 600 ft above sea level at Ranmore Common rrey though Hayes Common Kent which has an titude of only 250 ft., was almost clear for the whole riod; while at Blackheath at an altitude of only 100 ft. e tops of the buses were above the fog for part of the me There was hardly any wind and maximum mperatures ranged from 32° to 43°F The concentra ns of smoke and sulphur dioxide in the air of the ames Valley between Westminster and Beckton from o 2–4, were about the same as the averages for cember 1951 (when there was no intense fog) that is say about 23–71 mg of smoke per 100 c m and 10–21 ts of sulphur dioxide per 100 million parts by volume om Dec 5–8 however the comparable figures for oke were 103–375 *mg and for sulphur dioxide* 47–107 rts—about five times as much as usual In fact There no measurements for carbon monoxide over the riod but wherever there was dense and slow moving affic it probably became high anyhow at the level of r exhausts.

ere were fogs in other parts of the country—notably Glasgow *Leeds, and Salford, but none of them* attained the level of air pollution of the London fog, or lasted so long

Dr J A Scott, medical officer of health for the County of London recalled the results of a study *made earlier this year by Dr* W P D Logan,[1] which showed that in the two weeks following the fog deaths from bronchitis were 10 times as many, from influenza 7 times from pneumonia times from pulmonary tuberculosis 4½ times from other respiratory infections nearly 6 times as many as the average for the three weeks preceding the fog Other patients dying earlier than they would otherwise have done had disorders of the heart and circulation or cancer of the lung and an undue number of infants died from gastroenteritis presumably secondary to a respiratory infection Recent research has shown he said that sulphur dioxide and trioxide in concentrations in the air which are ordinarily non toxic, can when they are carried to the lungs in an aerosol, become exceedingly toxic and kill an animal in 4 seconds This information reached him from Dr Mary Amdur, who, with Philip Drinker and Mr W W Melville reports in our present issue some other effects of inhalation of sulphur dioxide by man While inhaling this gas all their subjects breathed more rapidly and less deeply and their pulse rates rose and one of them was so seriously inconvenienced that the experiment had to be stopped This study also shows that people who work constantly in atmospheres containing appreciable amounts of sulphur dioxide become tolerant of it but this immunity may be achieved *at the cost of a chronic inflammation of the upper* passages and we have no idea what its long effects may be

The risks to which fogs expose us all can be avoided in only one way—by producing less smoke Various measures directed to this end are now coming into action and the society have had a considerable share in promoting them "smokeless zones," for instance were the inspiration of Mr Charles Gandy, a former chairman Dr T Morrison Clayton medical officer of health for Coventry told the conference that at least fifteen local authorities have already obtained the necessary powers in private Acts to establish their own smokeless zones and others have the matter under consideration. The common council of the City of London have recently announced their intention of seeking statutory powers to establish a smokeless zone within the City[2] They intend to prohibit the installation of furnaces in buildings unless these are as far as possible capable of being operated continuously without emitting smoke But any impressive reduction of pollution Dr Clayton pointed out must depend on the extension of smoke*less zones to large areas which must be enlarged still* further over a period of years Manchester has made a beginning by proposing to extend its original smokeless zone to twice its present size and Coventry intends to do more than double its zone which was first established in March 1951 But many authorities *specially those not faced with excessive local smoke* problems are taking no action regardless of the fact that smoke knows no boundaries and that in these days of dispersal of industry factories may hatch out at any moment in their midst

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[1] *Lancet* 1953 i 336

[2] *Times* Sept. 23

In any case industry is not the only, or even the worst, culprit The domestic hearth, renowned though it may be for nourishing all the solid virtues, is itself no mean consumer of solid fuel one may almost say there is no domestic fire without smoke Indeed family hearths contribute some 900,000 tons—about half the —of our annual smoke output Those who think mokeless zones as applying mainly to industry ccept the awkward truth that if we are to abolish ous fogs, domestic fires must also be taken into This clearly places a duty on the house but it is hard for him to discover exactly at duty is Speakers at the conference offered suggestions first that he should burn only keless fuel, and secondly that he should fit his with modern improved grates which burn fuel completely than the older types In addition urged to use gas or electricity instead of coal whenever the weather permits But at once he nters difficulties The new grates are relatively esive—to buy, or to fit, or both—and so are gas ectric fires True, smokeless fuel can be burnt in in old-fashioned grate without adding appreci- to atmospheric pollution, but then the supply mokeless fuel is not adequate to supply every ehold, and moreover it is somewhat more costly y raw coal

is is surely a very silly dilemma We are in the t of fish whose stream is poisoned by the effluent actory our native element is being made noxious ; and already some of us have lost our lives we indeed fish, stringent regulations would at ome into force to prevent the nuisance It is an reflection that air pollution (with which past vers made several tinkering attempts to deal) probably grown steadily heavier through the uries, so that in this respect we have sunk, ration by generation, into slum conditions Our cities would have shocked our forebears as much heir drains shock us

t is surely time to help the National Smoke Abatement Society to clean the place up According to nmander C BUIST, Mr J O COOKE, Mr ERIC J VID, and Mr H H PROSSER, in their joint paper he availability and distribution of smokeless fuel, should concentrate first on the areas of heaviest ution—Greater London, the Black Country, south cashire, the West Riding, the Clyde, the Tyne, the Tees To eliminate domestic smoke in these , they say, something less than an additional 10 ion tons of solid smokeless fuels would be neces y, and it would be within the competence of the okeless fuel industries to produce that, say, on a n years' plan With support from the Government d local authorities, however, it would be possible to hieve this target in only four years, and to increase the tonnage to 15 million by 1962 Secondly, designs of appliances suitable for burning solid smokeless fuel should be available at reasonable prices and the makers of such appliances and distributors of smokeless fuel should provide an efficient service to advise the householder on the correct installation and maintenance of his appliance, and the kind of smokeless fuel to use in it

Householders have taken kindly to many of the new t f stoves and grates suitable for burning l some 2½ million of them were bought in 1952, so the task of persuading everybody to m them is probably not as serious as some ima Local authorities, it was also suggested, might compensation (as Salford has undertaken to do, to £2 per house) towards the cost of providing modern equipment in houses included in a smok zone, they can see, moreover, that efficient gr are provided in their own new estates Prof. F TYLECOTE, in his presidential address, urged on l authorities their duty of propaganda—by institut more regional committees, forming women's as tions, enlarging smokeless zones and creating ones, forming more "stokers' schools," arran exhibitions, meetings, and broadcasts, and urging th fellow authorities to join in smoke abatement schem Sir JOHN CHARLES, who delivered the fourth Des Vœ memorial lecture at the conference, emphasised great need for research He spoke of Profe DRINKER's plan to reproduce smog in a dis railway tunnel, and to examine its effects on volunteers The deliberations of the committee w has just been appointed, under the chairmanship Sir HUGH BEAVER, to examine the nature, causes, effects of air pollution and to consider prevent measures, may strengthen public opinion, and so the Ministry of Health's medical inquiry, but t wholesome dread most Londoners have of a recurr of last year's episode may well be our most powe friend One way of hastening useful action woul for more of us to join the National Smoke Abatem Society

Doctors and Inquests

WHEN his patient dies in circumstances which for an inquest, what action should the doctor ta His duty is none too clearly defined In tryin meet two interests—that of the registrar of and deaths on the one hand, and of the coron the other—he may satisfy neither

The doctor who has attended a patient in hi illness is obliged by statute to issue a medical ce ficate of cause of death "to the best of his knowle and belief," and to deliver it forthwith to the reg of births and deaths The phrasing of section 2 of the Births and Deaths Registration Act, 1 which has now been re-enacted in a consolida Act, is mandatory and explicit "that practitio shall sign a certificate" Again, under section of the Births and Deaths Registration Act, 19 "Every certificate of cause of death required to signed by that section [i e, section 20 (2) of earlier Act] shall be delivered forthwith by registered medical practitioner by whom the ce ficate is signed to the registrar " It is provided this subsection of the 1926 Act that, if an inq is going to be held, the notice to informant, wh the doctor is also required to complete, need no delivered to the registrar, but as the subs does not mention the certificate of cause of de the certificate presumably must still be deliv This is a change from the terms of the 1874 (section 20 [3]) which declared "Where an inq is held a medical certificate of the cause of d need not be given to the registrar, but the certifi of the finding of the jury furnished by the cor shall be sufficient" (At that time there was no n to informant) There seems little doubt, there at the Registrar General is entitled to the view[1] at "as the law now stands, the duty placed upon egistered medical practitioner [i e, to issue a medical rtificate of cause of death] appears to be unquali d, and unaffected by the fact that he or some other rson has reported the cause to the coroner or that inquest may take place"

Though certain persons have a statutory duty to form the coroner of a death the doctor is not one of ese—unless the patient was certified as insane The roner's claim on the doctor derives from common w, by which "it is the duty of every person who is out the deceased [which includes the doctor] to ve immediate notice to the coroner or to his officer to the appropriate officer of police," who then mmunicates with the coroner[2] This obligation wever, lacks legal force since there seem to be no ans open to the coroner to compel obedience has powers to deal with those who obstruct him the exercise of his duty but this duty, and its incident powers, cannot very well arise until he has en informed of the death The situation has been ther complicated by the growth of a practice which, ough without the sanction of law, has evident vantages many doctors when they cannot certify t the death was due to natural causes forthwith orm the coroner and withhold the medical certi ate of cause of death Obviously it is desirable that, en death is due to any unnatural cause this fact ould be brought to the notice of the authorities at earliest moment and it is clearly better to proceed this way—illegal though it seems to be—rather n permit the relatives to experience the frustration d delay inevitable when the information reaches the oner by the proper but devious route In cases ere death has been caused by a criminal act, cedural delay, even of only a few hours, can add preciably to the task of the police Delay must o be avoided where the circumstances call for a st-mortem examination refrigerating plant for the rage of bodies is scarce and without it post- rtem changes may develop which impede discovery the cause of death

n the existing circumstances it seems that the tor's proper course is to inform the coroner of any th which he cannot certify as due to natural causes, l also to issue a medical certificate of cause of th initialling statement 'A' to show that the oner has been informed. When the doctor does not w the cause the space reserved for this should marked 'not known' or 'uncertain' But the sent situation is unsatisfactory Whenever a tor is uncertain of the cause of death he should specifically responsible for reporting the death to coroner after which any further action so far the doctor is concerned should rest with the oner The coroner should be empowered to enforce nediate notification of circumstances which may essitate the holding of an inquest Furthermore e the coroner has been informed of a death, the tor should no longer be expected to issue a medical ificate of cause of death unless so directed by coroner

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[1] ntroductory notes and suggestions supplied with each book of forms of medical certificate of cause of death.

[2] ervis, J On the office and duties of coroners Revised by W B Purchase 8th ed., London, 1946

Annotations

CONDITIONED AND AUTONOMOUS NEOPLASMS

WHEN a chemical carcinogen is applied to the skin the resulting tumour has the character of an autonomous neoplasm in other words it arises and persists after application of the chemical has been discontinued. Two phases of genesis have been recognised: a phase of initiation in which a small proportion of the epidermal cells are permanently altered to latent tumour cells and a phase of development or promotion, during [illegible] the latent tumour cells multiply and induce vi [illegible] finally malignant tumours The phase of ini [illegible] requires a specific carcinogenic substance the ph [illegible] development can be brought about by the action eith [illegible] of a specific carcinogen or of a non specific irritant su [illegible] as croton oil This explains the long latent period betwe [illegible] the application of a carcinogen and the appearance of a tumour It also implies that the primary change takes place in the epidermal cell itself and not in the adjacent or underlying tissues though not everyone agrees on this During the development of carcinogen induced tumours there is a sequence of step like changes from normal epithelium to the subthreshold neoplastic state thence to papilloma, and from papilloma to carcinoma This has been called by Foulds[1] "progression" w [illegible] signifies not merely augmentation of size or of proper [illegible] already present but the development of new and ir [illegible] sible properties along the path of sequence of the ste [illegible] changes Progression may halt spontaneously for a [illegible] time at any point and it does not necessarily reac [illegible] end point within the life time of the host.

In certain circumstances tumours can be ind [illegible] which owe their origin to alterations in the host or the organ in which the tumour arises Furth [illegible] summarised much of the work in this field Admin [illegible] tion of goitrogens interferes with the thyroid pitu [illegible] hormonal relationship and results in the thyroid tum [illegible] by the following mechanism Thiouracil does not in [illegible] the thyroid cells, but it blocks their ability to synth [illegible] thyroid hormone (T.H.) thereby stimulating the pitui [illegible] to discharge an increased quantity of thyroid-stimula [illegible] hormone (T.S.H.) This causes tremendous hyperpl [illegible] and adenomatosis of the thyroid gland These adeno [illegible] can be grafted into animals whose thyroid glands [illegible] blocked with thiouracil but not into normal anima [illegible] The grafts, though dependent on the T.S.H. liberated [illegible] the thiouracil often metastasise to the lungs. Simil [illegible] mechanisms underlie the induction of tumours by inter ference with the gonadal pituitary relationship Wh [illegible] ovaries are grafted into the spleen of spayed animals, th [illegible] follicular hormones are transported to the liver by the portal vein and are there destroyed with a resulti [illegible] increase in secretion of gonadotropic hormones by t [illegible] pituitary This induces granulosa-cell tumours [illegible] luteomas in the heterotropic ovary Many of t [illegible] tumours still depend for continued growth on the pres [illegible] of excess of gonadotropic hormones but others bec [illegible] autonomous within the lifetime of the host

Furth also draws attention to the fundamental part played by hormones in tumorigenesis By analogy with the idea of the dual mechanism of initiation and promotion of tumours it might be supposed that these hormones act as promoting agents By this interpretation however there must also be an initiating agent in the many types of cancer induced by hormonal changes. With mammary cancer in mice such an agent can certainly be found in the Bittner milk factor; but there is no evidence clinical or experimental, for a similar initiating agent in the case of the gonadal thyroid, or pituitary tumours described It would thus seem that the malignant change in these cases takes place through disturbance of the physiological

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1 Foulds L. *Ann R Coll Surg Engl* 1951 9 93

2 Furth, J *Cancer Res* 1953 13 477

mechanisms by which the hormones produce their effects within the cell, but unfortunately practically nothing is known of the nature of these normal processes

Such observations as these have led to the concept of dependent or conditioned neoplasms, dependency being a phase in the progression to autonomous malignancy ins and his colleagues[3] have used this as the tical basis for advocating orchidectomy or treat with stilbœstrol for retarding prostatic cancer, and enalectomy (with suitable cortisone maintenance) for mary cancer In some cases the primary tumour regressed while the metastases have progressed, er cases both primary and metastases have ed These observations indicate that control of hormonal environment can prevent progression of pendent tumours to ever-increasing autonomy—perhaps a more rational means of saving life than either the urgical removal of established tumours or even the (still distant) prevention of tumours Once more the clinician is being helped by researches which might at one time have seemed academic and unrelated to the problems of one patient

FOOD IN BED

AMONG the useful activities of King Edward's Hospital Fund for London is the promotion of better hospital ring At an exhibition on Sept 30, at the Fund's ool of Hospital Catering (established at St Pancras ital, London, two years ago), visitors had the oppor of seeing hospital meals which had been cooked e students, *under the direction of the chef instructor,* of admiring the care with which they were served idea that food must *look* attractive is fast gaining und in this country, and the idea that it should also delicious must surely follow It was the confident of the chef of this school that his students' dishes ly looked good but had the right taste

the instructional kitchen every student has her own and tools, and four double gas cookers occupy the lle of the room Upstairs are common-rooms, a ure-room and a study, the students live out in gings arranged for them by the Fund Courses are nned for various groups—catering officers and those ut to become catering officers, head chefs and superndents, and cooks and assistant cooks The school o provides refresher courses for all grades of catering ff, arranges catering courses for hospital administrative d nursing staff, and provides a centre for lectures, monstrations, discussions, and conferences relating to aspects of hospital catering

Linked with the school is the Fund's catering advisory vice, which serves hospitals in all the four Metro litan regions, sending to them on request a catering viser, an equipment specialist, specialists in buying d costing, a designer draughtsman, and an adviser on chen management All these had taken their part in exhibition Plans by the designer draughtsmen ed kitchens of many hospitals as the Fund's team found them, and the same kitchens redesigned A model of one of these kitchens made it easy to see ow the movement of a few pieces of equipment or machinery, a partition, a new route for trolleys, and similar simple alterations had reduced pandemonium to order and lightened the load on feet and tempers A display of materials used in the structure and equipping of kitchens—modern types of flooring new types of laminated plastic trays, aluminium alloys for pans, lift cords, bowls, hand tools, and many other things—showed how rapidly design is advancing in this field All these things were explained to visitors by able and friendly members of the staff

Dr Charles Hill, parliamentary secretary to the Ministry of Food, whose short address, tossed together th [illegible] hand, agreeably served, and sauced with a dash of tart humour, would have done credit to any reminded members of hospital management comm (who seemed to be there in force) that they must think the lunch they were given daily in the board was the same as the one being served in the wards, urged them to send their cooks and caterers to school to learn from the instructors and from each o The school is a venture, he said, which deserves all *good will and publicity anyone can give it,* and warmly endorse that view

SUBDURAL EFFUSION WITH MENINGITIS

EFFUSION of fluid into the subdural space is *a recognised complication of bacterial meningitis* young children, and Ingraham and his associates[1] lately described 50 such cases In their series adopted the following indications for diagnostic subd "taps"

> "(1) Failure of the temperature curve to show a progr decline, particularly after 72 hours of adequate treat (2) positive C S F culture after 48 hours of adequate treatm (3) convulsions during the convalescent period, (4) convulsions at any time, (5) vomiting during the conval period, (6) gross neurological abnormality (7) the *impression that the course was unsatisfactory*"

When fluid was found, subdural taps were repeated for 7 to 10 days, no more than 20 ml of fluid removed at any one session Removal of the relieved undesirable symptoms "almost immediate *but despite this relief surgical exploration*, with the of removing encapsulating membrane, proved nec in no fewer than 42 of the 50 patients, and membrane was found

Analysis showed that in patients over the age years effusions were hardly ever found, but in the year of life 60% of all patients with influenzal, me coccal, or pneumococcal meningitis developed sig subdural effusions Ingraham and his colleagues that permanent neurological damage may result these effusions, and they therefore advocate (a) *nostic tap for any of the indications in their comp* sive list of signs, (*b*) repeated daily drainage of fluid, and (*c*) planned craniotomy, with wide ex the subdural membrane

This is a vigorous programme, and there is not enough evidence to justify its general applicatio Ingraham's 50 patients, 13 were treated before sub effusion was systematically sought in all patients, only 1 of these 13 children survived with intact men Of the 37 cases diagnosed during the systematic 22 have so far been followed for a year or more, and 16 of these 22 are rated as normal Ingraham com the results in the two groups and concludes that difference in results points to the value of his meth treatment There are grave objections to compar this kind Moreover, if untreated subdural ef commonly gave rise to cerebral damage, one expect poor results in centres where subdural rarely practised Yet there are many series on in which lasting cure of purulent meningitis has achieved in over 95% of cases, without common re to subdural taps It seems that if effusions occur these cases, then they regressed spontaneously ham's figures show that in more than two third patients whose effusions were tapped an encaps membrane developed later, and it seems possible the taps themselves provoked this undesirable react the meninges

There is no doubt that subdural effusions do purulent meningitis, nor that some effusions neurosurgical intervention Ingraham's routine ical aid in the treatment of at least 60% of small lren with *purulent meningitis There is no place for* tyro between the dura and the cortex a highly ed neurosurgical team will be needed to apply this nique But first a number of questions should be stigated Does the incidence of effusion vary with antibiotics employed with the route by which they given and with the dosage? Do all unaspirated ions persist as encapsulated foreign bodies com sing and damaging the brain beneath or do many ions regress leaving behind them merely some sions as harmless ichnolites? Only careful follow up ies can answer these questions The follow up must neasured in years or decades rather than months, mental defect is notoriously elusive in early child l, while epilepsy commonly matures silently between primary insult and the onset of seizures. [3]

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[3] [illegible] C. Bergenstal D M *Ibid*, 1952, 12, 134

[1] McKay, R J Ingraham F D, Matson, D D *J Am* *Ass* 1953 152 387

[2] Levine, S Z. Advances in Pediatrics. Chicago and Londo vol 4, p 15

he long-continued study of series of cured cases is a len that cannot reasonably be laid on the shoulders he overworked pædiatricians of this country and ies by a sequence of registrars or assistants are ilable Perhaps the responsibility may be brought to with the new Clinical Research Board

RESETTLEMENT OF DISABLED PERSONS

ARLIER this year the three Ministers chiefly concerned up a Committee of Inquiry on the Rehabilitation ning and Resettlement of the Disabled [4] in this itry and *its findings will be awaited with interest.* nwhile we cannot help thinking that the Ministry of our and National Service is presenting some of the s in less than due proportion Its *Gazette* [5] in speaking ie work of industrial rehabilitation units, has remarked , ' the modest experiment which started at Egham December 1943 can be said to have marked the nning of the discovery and use in this country of a set of sociological techniques More recently P H St John Wilson under-secretary in charge of k with disabled persons, is reported to have told the rnational Congress of the World Confederation for sical Therapy [6] that Britain s system of industrial abilitation and resettlement of the disabled is in ance of any nation s in the world—a statement which vely does justice to the pioneer work on resettlement e in Denmark and certain other countries years re there was any official machinery of the sort in tain, or to the current work of the Danish Invalidity rt which *particularly in the case of young disabled* ple [7] has much to teach our Ministry Mr Wilson etted that very few people realise that in this field ndeavour we are right out in front. This lack of reness of our achievements, he went on extends ortunately to doctors almost as much as to any section he lay community If the medical profession could only one per cent. of their attention to this sphere st of our resettlement problems would be solved.

: if Mr Wilson cares to read the history of work on resettlement of the disabled in this country he will l *that the medical profession was working on resettle*-it before his Ministry began to think about it. It the report of the British Medical Association Com tee on fractures [8] that stimulated the modern interest the subject—an interest which led in time to the ing up of the Interdepartmental committee which in n prepared the way [9] for subsequent administrative ion Nor must it be forgotten that long before the eption of the centre at Egham Mr F A Nicoll was using with conspicuous success at Berry Hill Hall in the *reablement of injured miners, the techniques subsequently* adopted at Egham or that the L.M S centre at Crewe the Seamen s Hospital at Greenwich and a number of other centres up and down the country particularly in the coalfields were doing similar work

Today 78% of all recruits to industrial rehabilitation units come from ' medical sources ' which does not suggest that doctors are unaware of the Ministry s work. *If they appear to be lukewarm in their enthusiasm for* its activities in the resettlement of *the disabled the reason* may sometimes be that they have been discouraged by its failure to give effective help to those patients whom they have referred to it. Of the hundreds of thousands of persons on the official Register of Disabled even allowing for those whose disability scarcely interferes with working capacity there are many who need help which they cannot in fact obtain In a large series of disabled persons studied *by Ferguson and MacPhail* [10] *few had received training in* new work suited to their disability yet of 728 who were out of employment when the study was made over 70% had worked less than half of the time since they registered as disabled persons from one to four years previously and 40% had never worked since registration Those who registered on the advice of doctors fared no better than the others The lack of suitable vocational training geared to a prospect of employment in suitable work at the end of training is particularly serious in the case of disabled young people.

One gap in our care for the disabled has lately been filled by the Ministry's offer to help local authorities to set up and maintain workshops for severely disabled people [11] Subsidies of this kind are already given for workshops for the blind and this provision is now being extended to sighted people who are severely handicapped But there is still a long way to go before the official machinery for the settlement of disabled persons in suitable work is as good *as it ought to be in this country* This is a matter in which there must always be a large medical element and to which medicine has undoubtedly a major contribution to make perhaps the findings of the present committee of inquiry may point the need for fuller recognition of the medical implications of disability and the employment of disabled persons than has some times marked the administrative approach even over a decade of full employment.

MICROANGIOGRAPHY

THE term microarteriography [12] or microangiography [13] refers to the technique of radiographing the contrast filled blood vessels of an organ in such a way that the finer vessels are seen when the radiograph is enlarged Microradiography a somewhat ambiguous term is the technique of producing radiographs that can be enlarged and the information obtainable from microradiographs of biological material has been well reviewed by Engström [14]

The difficulties of producing microangiograms limit *their usefulness to thin organs or sections of organs* and since relatively long X ray exposure times are needed, the method is at present virtually useless in the living subject unless the organ is very small and accessible The technique is useful because it may reveal the vascular anatomy of tissue a little thicker than that which can be conveniently studied by ordinary histological methods The tissue must not on the other hand be too thick for then the wealth of detail may be self-obscuring and it may be impossible to see the trees for the wood Microangiography depends on radio opaque contrast media and X rays, whereas more standard methods depend on coloured injection masses and light. The

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Smallpeice V Ounsted, C. *J Neurol Neurosurg Psychiat.* 1953 16 13
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erguson, T., MacPhail, A N., McVean M I M R C Memorandum, no 28 H.M Stationery Office, 1952
Brit med. J 1935 suppl. Feb 16 p 63 Feb. 23 p 69
Home Office Ministry of Health and Scottish Office. Final Report of the Inter Departmental Committee on the Rehabilitation of Persons Injured by Accidents. London H.M Stationery Office. 1939

[10] Ferguson, T., MacPhail A N *Glasg med. J* August, 1953 p 343
[11] Ministry of Labour Circular D P 636/3 51
[12] Barclay A E. Micro-Arteriography Oxford 1951
[13] Bellman S *Acta Radiol., Stockh.* 1953, suppl 102
[14] Engstrom A *Physiol Rev* 1953 33 190

injection of any contrast substance into the vascular system during life may fail to show individual vascular channels if, at the moment of observation, the contrast medium is not flowing through them in sufficient concentration, or if with the method of display the definition is inadequate Similarly, injection masses in necropsy material may for various reasons not demonstrate a given vascular channel, even though this is patent

Microangiography may often be a useful ancillary method,[15 16] but equivalent results are usually obtainable by other techniques Should it prove possible in the future to take rapid serial angiograms of organs in life which can then be enlarged, then this technique may sometimes yield information that is otherwise unobtainable

ASSESSING A COUGH SUPRESSANT

The obvious way to test the value of a cough suppressant drug is to give it to patients with coughs and observe the result This is the method that Cass and Frederik[17] have adopted in a trial of the new antitussive agent, dextromethorphan But their study shows that even such a simple experiment must be conducted with extraordinary care Their plan was to have the patients themselves, their nurses, and their own ward doctors record the severity of the cough four times daily, on an arbitrary numerical scale from 0 to 4 During a 45 day period the patients received medication four times daily with various substances, the nature of which was unknown to themselves and to the other observers These substances were dextromethorphan hydrobromide, codeine, and an inert tablet —the last two representing positive and negative controls Three batches of each substance were prepared, and each of these nine batches was identified solely by a code number Every patient received successive 5-day courses of each of the nine batches, the order in which they were given being decided at random and differing for each patient For a study on this plan to be statistically irreproachable, the nine batches should be given in every possible sequence, but this requires the participation of 362,880 patients Cass and Frederik were content to screen 1400 patients, from whom they selected 160 as having a cough of suitable degree and duration For one reason and another in only 65 of these patients were records completed The observations made by the patients and nurses had to be rejected because of gaps This left only the records made by the ward doctors, and even these were not above suspicion One such observer is reprimanded by the authors for cheating—he apparently kept a box score of his observations in an attempt to decode the drugs prematurely—but, once this was dealt with, " no personal feelings were allowed to colour any of the observations " Eventually a series of over 11,000 numbers was obtained, representing the cough severity in 65 patients for four periods a day during 45 days It might seem that the effectiveness of the three substances could then have been compared by adding all the numbers obtained for cough severity for each substance in turn But the statistical analysis showed that such a course would yield a fallacious result, because the differences in cough behaviour between individual patients receiving the same medication were greater than the differences in the same patients receiving different drugs When allowance was made for this variation by an appropriate mathematical manipulation a further difficulty arose One of the three batches of dextromethorphan was found to be apparently less beneficial than the placebo This evidently was the price Cass and Frederik had to pay for reducing the number of patients belo statistical ideal random selection had resulted in particular batch of drug having followed codeine frequently in the sequence of administration than the other two batches But the conclusion finally d from this study cannot be seriously questioned it is dextromethorphan hydrobromide in a dose of 4 mg an effective cough suppressant, with about half effectiveness of 17 mg of codeine Cass and Fred think that 10 mg of the new drug may have same effect as 17 mg of codeine

The pharmacological interest of this work is that d tromethorphan belongs to the new series of morph substances the members of which exert some or a the actions of analgesia, central depression, addic liability, and cough suppression The synthetic anal racemorphan (' Dromoran '), the best known member this group, is related to dextromethorphan chem much as morphine is related to codeine Dextrometh phan has been shown to be devoid of addiction liabili and to cause no central depression[18 19], and this la study confirms that the definite antitussive action o 4 mg dose of the hydrobromide is unaccompanied side effects

THE SHORT BIRTH CERTIFICATE

The fear that short birth certificates would be so only by those whose parents were not married, and would become tantamount to certificates of illegitima has proved to be quite unfounded A subcommi appointed by the Magistrates' Association,[20] to inq into their use, draw attention to the study made by Registrar-General between the end of 1947, when certificates were first issued, and 1951 This showed for local offices, the proportion of short certificates from 40 5% of the total issued in 1948 to 62 5% in 1 At Somerset House the rise was less striking ove same period from 26 2 to 30 4% , but even th sufficient to ensure that the certificates are not l sought by the illegitimate alone From the end of until the end of 1952, about 4 million short certific were issued , and there were only 2 million ill people in England and Wales at the time, not all of had had occasion to get birth certificates Thus evident that legitimately born people had felt no di about taking the shorter form

The subcommittee are still concerned, however, ab the position of foundlings, whose certificates car statement that they were born " on or about " such such a date , and this might reveal them as fo to the informed or the curious Similarly, short cert cates issued to children who have been adopted give the country of birth and not the district, which c betray them as being adopted children The comm is considering ways in which these aberrant type certificate may be brought into line, thus supporting principle of a fair start and no favour

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Sir Edmund Britten-Jones, F R C P, physician to the Adelaide Children's Hospital an former vice president of the Royal Australasian Co of Physicians, died on Sept 30 at the age of 64

Prof Edwin Cohn, of Harvard, whose work on fractionation of blood-plasma has found many valu applications in clinical medicine, died on Oct 1 at age of 60

We also regret to announce the death of Dr Flo Sabin, of the Rockefeller Institute, long disting for her work in hæmatology

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15 Ardran G M *In* Modern Trends in Diagnostic Radiology Ed J W McLaren London, 1953 , series II chapter v

16 T[illegible] Harrison, M *J Bone Jt Surg* 1953 35B 424

17 [illegible] Frederik, W S *New Engl J Med* 1953, 249 132

18 Isbell H Fraser, H F *J Pharmacol* 1953 107, 524

19 Benson W M, Stefko P L, Randall L O *Fed Pro* 11 322

20 Thirty third Annual Report 1952–53 Pp 39 Obtainable the secretary of the Magistrates' Association, Tavistock South, Tavistock Square W C 1

Special Articles

URTHER ADVANCES IN PATHOLOGY *

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HE hope with which we peer into the future at any
is apt to be tinged with a certain amount of anxiety
both emotions are heightened when evolution is
d At such periods it is useful to examine the main
of evolution and to discuss them as frankly as
ible. By so doing we may in some fashion shape
course and avoid certain pitfalls

o-one is likely to challenge the assumption that
ology will continue to make important advances
he near future in respect of acquired knowledge
n however, less concerned with this aspect of progress
he present moment than with the practical problems
ted by the growth of knowledge, and consequent
ialisation I propose to discuss some of these
blems, and to suggest a few possible ways of mitigating
difficulties that already threaten the organisation
ur various branches of study

HISTORICAL BACKGROUND

he development of pathology up to the present
tury and *its subdivision into different branches, is a*
iliar story and therefore one upon which I do not
pose to dwell at length It will suffice to remind
of a few facts.

orbid anatomy is as old as medicine itself and until
middle of last century was practised by the clinician
was thereby enabled to correlate his observations
the bedside with the naked-eye appearances of dis
ed organs Keen observation backed by intelligence
ded a rich harvest at the hands of such as Richard
ght, Addison and Hodgkin—to mention a few The
jection of morbid anatomy to the subtler processes of
opathology, and the microscopic analysis of changes
with the naked eye led to the establishment of
oratories with all their paraphernalia including the
rarchies *of academic and technical staffs* This
ed the way to the transference of post mortem dis
tions from the hands of the clinician to those of the
hologist Not without local struggles however
ause many clinicians set great store by this first
d experience In the early part of the present
tury the physicians at the London Hospital habitually
formed post mortem examinations and, in that
acity were dubbed visiting pathologists. Their
its lacked punctuality and their dissections were not
ays edifying either to the medical students or to the
hologists who had to report upon the results! My
decessor Prof H M Turnbull insisted upon
ctuality and whether it was due to this ruling
ich I am sure he enforced) or to the meticulous
hnique which he imparted from his previous studies
Dresden or perhaps to an access of wisdom it
hard to say but the attendance of the visiting
thologists ' gradually tailed off After the first
rld war there was only one to my recollection who
t in a regular appearance for this purpose But his
ctuality and standard of performance were both high
was a welcomed ' visitor

At this time it was rather fashionable to write off
topathology as effete The objects of our study
neath the microscope were held to be conglomerations
artefacts moreover the Germans had mapped out everything of importance, and little remained for discovery Never was a judgment more erroneous! At the present time new fields are opening out in histochemistry and cytochemistry and new kinds of microscope reveal structural details that were hitherto unknown Fresh aspects of disease are constantly appearing for various reasons they demand vigilance and adequate investigation.

The rudiments of what we call *clinical pathology* are of equal antiquity if we include the gross examination of various secretions and excretions But clinical pathologists and the laboratories sacred to them are of recent date They often started their existence in a hole and corner fashion within the larger hospitals at the instigation of honorary consultants who realised that such laboratory services could be of value to them Such at any rate was the mode of origin at the London Hospital The amenities provided there have been described by the late Sir Philip Panton, in his *Leaves from a Doctor s Life*[1] as ' a single room together with a staff of one extremely ignorant technician When it is recalled that this was the meagre beginning some fifty years ago the rate of subsequent development has been startling In particular we may note the extraordinary importance of hæmatology which bids fair not only to establish itself as a separate discipline but even to indulge in subdivisions of its own

In *bacteriology* we have witnessed a similar kind of growth and specialisation The late Professor Bulloch who occupied the chair of bacteriology at the London Hospital Medical College from 1919 to 1934 used to give lectures in general pathology As well as being an eminent bacteriologist he was in fact a sound pathologist with a wide knowledge of the various branches as they then existed. In his early days he was a student of neuropathology, and he retained his interest in the silver impregnations for neurofibrils and axis cylinders I possess an elegant preparation of Auerbach s plexus made by him as a by product when he was working on the sterilisation of catgut a few years before his retirement But today the academic bacteriologist may devote himself to the study of viruses, or immunology or to some other aspect of microbiology His terminology is so specialised that it is often difficult for others to take an intelligent interest in his scientific communications His opening gambit is often a complicated table thrown upon the screen with the minimum of preamble, which (to quote the late Prof E H Kettle) provokes an antibody reaction in the unversed beholder! I shall revert to this matter later

Chemical pathology came relatively late upon the scene Founded upon organic chemistry which itself underwent systematic development in the 19th century the subject was still in embryo until after the first world war when colorimetry came into its own and greatly extended the scope of chemical analysis of the body fluids. A number of other refined methods of analysis have recently come into use Chemical pathology is still engaged in the struggles bound up with its expansion, and emancipation from a position subordinate to clinical pathology

THE TENDENCY TO SUBDIVISION

At the present time therefore we are all fully aware of this steady and rapid growth of the various branches of pathology and the tendency of those branches to *subdivide into further subgroups or specialties* We recognise also that this tendency is not peculiar to pathology but is a general feature of medicine and indeed, of other sciences The situation in medicine as a whole has been examined by Sir Russell Brain in his annual oration to the Medical Society of London[2] He traces the ways in which the various clinical specialties have become separated—a process of disintegration and differentiation Side by side with this there are certain points at which reintegration takes place, owing to the necessity for mutual aid in diagnosis and treatment amongst the specialists

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* residential address delivered before the Association of Clinical Pathologists on Oct 2

[1] Panton, P N Leaves from a Doctor s Life. London 1951 p 131.

[2] Brain, W R. *Lancet* 1953 i, 959

We have heard much, in recent years, of the necessity for integration and synopsis in relation to medical education But, although we may have subscribed in theory to the proposals made by the learned authors of sundry reports and memoranda, I submit that so far little attempt has been made to put the advice into practice This is explicable because a reasonably integrated presentation of medicine, including of course pathology, is not feasible unless those responsible for the growing points of knowledge—namely, the active researchers—will undertake the responsibility for integration amongst themselves This point needs further elaboration

THE SPECIAL PATHOLOGIST

Since the practice of pathology necessarily goes hand in hand with clinical medicine, it follows that special lines, for example, neuropathology and ophthalmic pathology, have tended to be segregated in hospitals devoted to these specialties In past decades the pathology at such hospitals was often unsatisfactory because the office of pathologist was occupied by the aspirant to a clinical appointment He therefore used the laboratory appointment, which was generally part time, merely as a stepping-stone The main brunt of the laboratory work was borne by a senior technician who often acquired authority to a formidable and unhealthy degree ! This arrangement has properly given place to a system of full-time and permanent special pathologists Their segregation, however, carries with it certain dangers to the interests of pathology as a whole, and this, I think, applies particularly to histopathology In the first place they may fail to appreciate the importance of correlating their observations with the pathology of the body as a whole They sometimes in fact become curiously detached in this respect I once overheard, in a neuropathological laboratory, a somewhat contemptuous reference to the extraneural tissues as "the trunk tissues" Another menace lies in the elaboration of special nomenclatures which tend to alienate their users from pathologists in general Ophthalmology is a conspicuous example of this habit Amongst neuropathologists there is an affection for German terms, or for literal renderings of German expressions, in their special nomenclature This is confusing for others and appears to me absolutely unnecessary There can for example be no excuse for the use of the term *Gitterzell* when the perfectly good equivalent of "foam cell" is ready to hand, or for the description of a loss of neurones from some part of the nervous system as "an outfall" I would plead therefore for the simplification of nomenclature, and the application of terms in general use to special instances whenever possible And this recommendation applies not merely to histopathology, whence my examples are taken, but to all branches of pathology The alternative development will simply lead to a confounding of language—in other words Babel—in which none will understand what the others are saying

Were it possible to wipe the slate and start afresh, there would be a strong argument in favour of the development of such special lines as pædiatrics, neurology, ophthalmology, and so forth in intimate association with institutions concerned with general medicine In modern hospital planning this kind of centralisation is in fact favoured The arrangement would permit of a centralised department of pathology in which special pathol[illegible] could pursue their separate lines to the mu[illegible]ntage of all From personal experience I can testify to the advantage of this, since I practised neuropathology as a special line both general pathological department and, later, independant laboratory segregated in a neuro unit The latter arrangement carries certain undo benefits both to the pathologist and to the clin But on balance, since there must necessarily be a c between these alternatives, I think the greater adv lies in having the neuropathologist (or any other sp pathologist) incorporated as a unit of a larger de ment of pathology, with whose personnel a exchange of views and criticisms is possible It be recalled that this was also the recommendatio the Goodenough Committee in 1944[3]

This recommendation needs further empha account of the growing tendency towards speci tion on the part of hospital clinicians, and the fact these clinicians are turning with increasing eage towards the laboratory for help They recognise that histopathology, far from being effete, has great potentialities in illuminating the obscurer co of clinical study The close coöperation of clinician pathologist has indeed become more than ever tive Unfortunately, however, the routine hos pathologist has neither the time nor, in many resp the necessary background of knowledge to satisf these requirements He may, and often does, de such time as he can spare to research in one p specialty Thus the only satisfactory solution be the employment of as many pathologists as importunity of clinical specialists may demand for solution of their problems But neither space money are available to implement this either n in the immediate future

SCIENTIFIC COMMUNICATIONS

I must turn now to other questions arising directly from research and, in particular, the c munication of the results of research to others. We faced with difficulties arising both from the rapid in the membership of our societies, and from the character of the communications read at meet The Pathological Society of Great Britain and Ire is now so bulky that it is usually necessary to split programme in two concurrent parts, thus divi the bacteriologists from the rest Both are thus dep to the detriment of both But this arrange loudly regretted by so many members of this soc is a kind of segregation that is sometimes activ sought by other groups in pathology Thus a few ago there was a bid to set up a separate section hæmatology in the Royal Society of Medicine. Ma of us felt this to be undesirable since it would weakened the section of pathology Again, wi recent months, an Association of Clinical Biochem has been created While the council of the Associ of Clinical Pathologists has formally welcomed this step, it is ardently hoped that it will in no way im the participation of the biochemists in our more ge meetings

There is of course nothing to prevent any group specialised workers from forming a society for purpose of discussing their own particular problems, much profit may be derived from such discuss But I hold that no specialised society of this kind sh detract from the membership of, and active participat in, more general societies We may indeed visu a possible evolution of our societies whereby those more general character and membership may come exercise their most important function as a medium the interpretation and correlation of the growing po of knowledge I look forward, in short, to a phase velopment in which experts will probably herd together numerous small but highly specialised societies They ll doubtless air their views in terms incomprehensible others But the more clear headed and thoughtful these experts should be able to present the results a general gathering of pathologists, using terms that e majority at least can understand and relating any vances made both to basic principles and to cognate sciplines. In the meantime we may flatter ourselves at the Association of Clinical Pathologists incorpora g as it does all the main branches of pathology that applied to clinical medicine is of the greatest value holding together our various interests and in main ning a nice balance between academic and non demic practice

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[3] Report of the Interdepartmental Committee on Medical Sc H M Stationery Office 1944, p 141

ROUTINE AND RESEARCH

At this point I should like to say a few words to patho gists of the non academic category Perhaps they metimes feel that they are overburdened with routine rk and that research is outside their orbit There , however *notable exceptions, as we well know* e combination of routine work and research is in elf admirable and all routine workers should command fficient technical and other support if they are inspired carry out original investigations. In many instances s support is wholly inadequate I gather however n the columns of the *Manchester Guardian*,[4] that the nister of Health recognises the prime importance of veloping laboratory facilities in order that this country y not fall behind in the field of investigation We y hope therefore for further expansion when restric ns on capital expenditure are relaxed

It is perhaps insufficiently appreciated that academic thologists, on the other hand are often too over rdened with routine duties to give such attention to *ginal work as is demanded by the universities* But is common knowledge that advancement is only ined by means of substantial publications Hence bloated condition of our journals and the congestion editorial desks. In fact Alan Gregg[5] states: I ow of one department in an American University ere the value of a man was estimated by the number pages he had published divided by the number of ars he had possessed the PH D degree It was a partment of psychology Research is surely a oured conception at the present time, and an umbrella much that is inept On the other hand there exists inspired researcher who would worthily fill a chair t who rejects this proposition from the knowledge t acceptance of professorial status, with its inevitable rden of administrative work would prove crippling his main interests Sacrifice of position and financial ward is the penalty for his decision.

THE WHITE PAPER AND ITS CONSEQUENCES

Such a situation calls for remedy and we may hope m the recent white paper on clinical research[6] that solution is within sight In the first place it recom nds arrangements for decentralisation enabling spitals to promote research with the greatest possible edom and without detailed supervision Secondly rejects the principle that the research worker should paid less than the clinician thus the man who has genuine flair for research could look forward to the spect of a research career without the sacrifices viously entailed

The various branches of pathology must surely be ected by these proposals There are few forms of clinical research that do not involve extensive laboratory investigations and one may perhaps envisage the future director of research as a person who has been so well trained both in the wards and in the laboratories that he can coördinate the researches of juniors who are working in either In the sphere of pathology we probably are all acquainted with the man who has the ability and inclination to do whole time research but has no wish to be segregated in an institute which is entirely detached from hospital work His interests lie in the application of his observations to clinical problems He must therefore attach himself to a hospital to gain the stimulus and the opportunities required But at the present time there is virtually no provision for a worker of this kind. A few research fellowships are available here and there their tenure is usually limited, and the salaries attached of an order that anyhow opposes long tenure It is obviously unreasonable that whole time research should entail celibacy These research fellowships should serve a valuable purpose as a testing period for those who show promise and are gifted with the various attributes that we regard as desirable in a prospective researcher But when the testing time is over and a reassessment shows that the candidate has proved himself a permanent post at advanced remuneration should be his reward. Reverting to the white paper we must like Mr Micawber hope that something will turn up !

Finally I should like to notice the recommendation of the white paper that the central research organisation should be empowered to make when necessary arrangements for work abroad Either individual researchers or units might profit in this way The profit would also extend to the centres visited in the case of those that are geographically isolated or lie in the more backward countries This conception is in close harmony with views expressed this summer at the Cambridge Congress of Commonwealth Universities An increasing degree of free movement of scholars between these constituent universities would confer an inestimable benefit not only upon the scholars themselves but also upon the growth of mutual knowledge good will and understanding In pathology we are aware of many racial and geographical variations in the pattern and kinds of disease *These demand investigation not only for* their own sake and for the sake of those who suffer thereby but also because their study would doubtless lead us to a better understanding of our own diseases

Our outlook and teaching in this country are far too parochial; the enrichment gained by periods of work abroad is, in my view a target that we should set as a desideratum for all Before settling down it would be no bad thing if it were obligatory for every young pathologist to undertake a spell of study and if possible research in some other part of the Commonwealth as part of his training Were this accepted as a general rule the fear of being forgotten, or of slipping off the academic ladder would lose its force And doubtless it is that fear as well as the present absence of any proper financial provision that has inhibited the otherwise bold spirit from embarking on a venture that might prove so profitable to himself and to human society

THE ASSOCIATION OF CLINICAL PATHOLOGISTS

There are doubtless many aspects of my subject that have been left untouched, but I have *said something* of those that appeal to me as most important And I have chosen this occasion for the purpose from my conviction that it lies more within the power and scope of this association than of any other body to maintain the integrity of pathology in the face of growing diversification

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Manchester Guardian Sept 23, 1953, p 3.

regg, A Furtherance of Medical Research. New Haven 1941; p 165

linical Research in Relation to the National Health Service. H M Stationery Office 1953.

The Widdicombe File

III ORGS ?

MY DEAR WHIDDON,

I owe an apology to you and to your house surgeon To him because I rebuked him more sharply than mere ignorance deserved, and my only excuse can be that his youthful appearance—is there still a minimum age for medical registration ?—brought out the old dominie in me To you because in rebuking him I usurped your locum parentis (or locus ?—a nice point of usage) I should have remembered that it is your custom to include good manners and common sense as part of the education of the young surgeon

The young man reflects little credit on his previous teachers I am accustomed to those who use my laboratory as a sort of penny-in the slot crystal ball from which all the answers to their silly questions may be obtained in a twinkling, but on that morning I was out of sorts and jibbed at the specimen of fæces accompanied by the bald query "Orgs ?" Do you blame me if I returned the immediate answer "Present" ? I hoped that by this brutality I might impress on his mind that useful answers are possible only to useful questions—but the blame is not his I have little doubt that bacteriology is the worst taught subject in the curriculum It takes up a good deal of time which the student might spend better in the wards and leaves him with some ill-digested applied botany, a lot of names learned by rote, and the illusion that if he sends any specimen to the laboratory he will receive the correct diagnosis on a plate without further effort If it is taught apart from general pathology —as it usually is—he forgets that bacteria by themselves are no more harmful than puddocks in a pond Because they are "classical" he learns a lot about typhoid and plague bacilli and the pneumococcus as parasitic members of the vegetable kingdom, but about whitlows and inflamed tonsils very little and he seldom knows how to immunise his own child against diphtheria Do you still devote much time to teaching the surgical treatment of aneurysms ? Because bacteriology in the medical school is divorced from medicine and surgery it is only after years in practice (or six months as your H S) that he learns that the findings of the laboratory are no more than physical signs, of the same order of truth as those which he detects with his own eyes and hands Their diagnostic value resides not in any single one of them but in the sum total

* * *

If I were to return to teaching perhaps I could not do much better I am not frightened of the vested interests of those who earn their bread that laborious way or of those who collect the fees from examination candidates The truth is that I hardly know enough bacteriology in its applications to medicine to let me teach it without a good deal of misgiving If I am injecting a mouse with anthrax bacilli and I let the needle slip into my finger I know I have done a foolish thing, but I also know from experience that I am not bound to suffer an infection Do you remember our happy meeting—happy for me at any rate—in Deolali on our way home from SEAC ? We both wished to buy some ornamental trash as evidence that we had in fact seen the glorious East, but the bazaar was out of bounds because there had been two cases of bubonic plague there Now I will bet my boots that that bazaar held all the textbook essentials for a thundering good epidemic—humans and fleas and rats beyond the dreams of a rodent exterminator's avarice—and there were just two men suffering from plague [illegible]hen I used to give my lecture on plague to the [illegible] I used to tell them to read *Martin Arrowsmith*, but I am glad that none of them me the questions I asked myself in that bug-i tent

Contrariwise the other day I saw an outbr infectious disease which should never have happe all—according to the books An entire resp middle class family were prostrated with a sal infection The housewife set a standard of cle which I seldom see in my own home (I trust discretion), they had had no visitors, they eaten elsewhere, their food came from the sam as did their healthy neighbours', and they touched duck eggs or mutilated meat or any suc Students learn about natural and acquired and minimum infective doses I wonder ho teachers add that as far as our knowledge go none of these things explains many of the phenomena associated with infectious disease. I am right in saying that no-one really kno touches off a major epidemic Greenwood, w and thought more about these things than m postulated besides the parasite and its host quid—which is a decent and scholarly way of ignorance

* * *

But these are more than subjects for academ tion Twice in recent weeks I have seen in our own maternity block which underlined ignorance

The first arose from that rarity of these days, puerperal infection with hæmolytic streptococ else was ill, patients or staff, but Matron praiseworthy anxiety lest one of her nurses been the source of infection I had foreboding and no doubt she put down my hesitations I yielded—of course—and we looked at the nose swabs from the twenty-five nurses an who staff the block Eight of them harboured streptococci in their throats, but—and this of hard work for somebody else—none of th the same "type" as that in the original suff fact, we never found whence her infection ca book one of the nurses would have been a who had been on duty in the labour ward w similar infection occurred nine months ago problem had left us with another Here we carrying a potentially dangerous organism in in the presence of patients traditionally s severe infections If we took them off du would have to close, perhaps two If we di should look worse than mugs if a seco occurred The epidemiology of puerperal received the attention of some pretty brains since Semmelweis, but I could not ba to Matron on anything better than an guess of the risks involved In the en carriers stay on duty, chewing penicill kept them out of the labour wards infections were noticed Matron thinks of me

A week or two later another patient ra after delivery, and, as is usual and prope swab from her cervix I found a little pus culture grew *Bacterium coli* and *Streptococcu* staff, unasked and probably unwisely, foun that both of these were sensitive to ch and with this the patient was treated He way, had subsided before my report rea Were these organisms the cause of her fe did they justify the use of a drug which its dangers ? After the event the answer question is clearly 'No", but the first is a difficulty which I meet every day T e normal inhabitants of the bowel but both are capable causing infections elsewhere in the body Neither is normal inhabitant of the vagina, but my faint memories obstetrics suggest that even the best-conducted labour ves some opportunity for the mechanical transfer of ese organisms from the anus Here we found them sociated with pus, and in my simple way I have always sumed that pus is evidence of an inflammatory reaction oes the trauma of childbirth produce such a reaction is the pus evidence of infection albeit a low grade e? At this point I begin to think about angels on a edle's point. We just do not know if the fever was ue to infection with these organisms and I believe the ouse-surgeons erred in assuming that it was In fact gave more weight to our report based on ' scientific " ethods than to the plain fact that by the time he received the patient was very well indeed. I see this impulsive ge to treat first and think afterwards so frequently ace we have had the omnipotent antibiotics that I spect some of our junior colleagues of believing that e only good bacterium is a dead bacterium

* * *

The medical wards plague me with requests for the evalent organism in sputum I wish I knew how is heresy arose. Much of what is labelled sputum ' of course saliva but I will overlook the difficulties hich arise from this Until I am blue in the face I have inted out that the prevalent organism as seen in a ained film of the material is seldom the organism most umerous in my cultures Let me choose the medium d I will give them pneumococci or coliform bacilli or asts for an answer The physician's assumption is, I ppose that the most numerous organism is the one hich is causing the patient's illness and that if he can terminate it with this or that expensive antibiotic the or chap will get better I am not competent to discuss e second part of the argument but my experience has en that the commonest effect of antibacterial treatment one has been to replace one organism with another most as likely to cause disease If I judged by numerical evalence alone I would not give much weight to the bercle bacilli in an open cavity

In appraising the bacteria in sputum we are guided by e analogy of infections elsewhere in the body and by e dogmatic simplicity of the textbook which labels me organisms pathogenic —pneumococci and influ za bacilli—and some saprophytic There are, I lieve very few organisms—tubercle and perhaps thrax bacilli—whose presence in the sputum is evidence r se of disease The great majority—whatever their bels in the book—can enjoy a parasitic life in the human ndpipes if the environment is suitable. In the sense at a staphylococcus causes a boil I rather doubt if y organism causes chronic bronchitis If I am ong I do not know of any evidence derived from rasite or host which will let me put the blame on the ght shoulders. Perhaps they all have a share in the ork We know next to nothing about bacterial symbiosis d I sometimes wonder if the flora of the bronchial tree es not play a part akin to that of the bowel—a part gely beneficial to the owner of the tree Perhaps the ect of a few doses of penicillin on the man with chronic onchitis is rather like that of a few days on yoghourt— stirs up the flora like a gardener with a hoe

* * *

Being a hospital bacteriologist is a very difficult job the golden age of bacteriology—say up to 1906—it s the Pasteurian dogma of specificity which made the lence so exciting and so satisfying Like causes like ere are two patients who suffer from what appears to the same ailment the microbe—an old word not used enough—common to both will be the responsible agent (The biggest blob was beriberi, and the evidence for its infectiousness was better than most people think) Nowadays specific infections seem regrettably, rare We bacteriologists deal mostly with material from bronchitic chests and dirty wounds and—saving your presence—ancient sacculated bladders. Once upon a time we used to spend our days searching for specific organisms—typhoid bacilli or gonococci—to confirm half made diagnoses now we look for an unknown organism which will give a guide to treatment We have all the elegant equipment we can reasonably want We use methods of beautiful refinement and we seldom meet any organisms to which we cannot give a name with a clear conscience Our chief trouble is, I think, that our methods were designed for other ends. Some as I have said, are meant to reveal a specific organism which will confirm a diagnosis —and some work of this kind will always be with us Some—and these are the most refined—were designed to help the epidemiologist. Improvements in culture media let me detect the scanty typhoid bacilli lurking in the carrier's bowel, and for this purpose are better than the older and simpler media When we used to use these I have no doubt that we missed many carriers, but we were no less successful in confirming the diagnosis in an established case of enteric The price which we pay for detecting the single typhoid bacillus is the likelihood of overlooking other organisms of importance which will not grow on these eclectic media This is probably why we were rather slow to spot that certain severe infections of infancy are due to a strain of *Bact coli* indeed I have heard that these first came under suspicion by reason of the smell of the fæces rather than by the orthodox methods of the laboratory (Of course the nose is useful in the laboratory—but don't tell anyone I said so) Epidemiology is an almost unhealthily fascinating subject but its charms have tended to seduce the hospital bacteriologist from his job—which is to assist in the diagnosis and treatment of the sick.

Our other trouble arises from the fallacy that certain organisms are pathogenic and the others are not You can tell the pathogenic ones because there is a list in the textbook, and if I find one in a specimen it must be the cause of the patient's disease. If I cannot find one the disease is due to a virus or is the province of the trick cyclists Of course this is plain biological balderdash but you would be surprised how often I meet it. Pathogenic and saprophytic ' are useful words in writing reports—I use them myself quite frequently—but I really think that they are applicable only to one organism in one site in one patient. I have stroked a lion—with misgivings—and have been bitten by a rabbit.

What we usually lack is evidence of the pathogenicity of any one organism in an individual patient at a given time There are exceptions. The most convincing is the rise in the titre of antibodies in a patient's serum during the course of illness—especially if the same organism can be found somewhere about his person It is an old method which might repay examination if applied to some of the infections which appear to be non-specific.

I am not so far sunk in doubting apathy that I attribute no importance to the meningococcus in the purulent cerebrospinal fluid or the streptococcus in the blood of a patient with the signs of endocarditis I do not really doubt that hæmolytic streptococci cause tonsillitis but I wish I knew if non hæmolytic streptococci do much the same thing I rather think that the botanical origins of our subject and the charms of our technique have led us for too long to look harder at the parasite than at its host—and the second is the way for future advances

Perhaps these will never come Unless we are careful I forsee that we shall be asked to do no more than discover to which antibiotic any infecting organism is sensitive their vulnerability will be more important than their names Indeed today their names are wanted only as a rough guide to treatment Perhaps this is the right way to deal with non-specific infections—it was you who taught me the virtues of Eusol dressings—but it hurts my professional pride I said that bacteriology was difficult I meant useful bacteriology Nothing is easier than to report that a specimen contains these and those organisms and nothing is harder than to persuade myself that I am not drawing a long train of stinking herrings across the paths of truth

* * *

On this poetic note I will end my lamentations and add yet another apology for letting off so much steam (? hot air) and all because I hinted to your house surgeon that he is an ignorant booby He is that and all, and I know that you will exert yourself to correct his failings If you will bring him in to laboratory tea on your next operating day perhaps I may be allowed to help ?

Yours very sincerely,

HARRY HAWKE

Medicine and the Law

Mistakes with Anæsthetics

Two fatal mistakes in the dispensing of anæsthetics were recorded in September

In the first [1] a girl of 19 was undergoing an operation for goitre The surgeon ordered as a local anæsthetic an injection of a solution containing 6 grains of 'Novocain' in 7 ounces of normal saline to which adrenaline was to be added shortly before use As he was dividing the tissues to expose the swelling in the thyroid, a fit developed and the patient collapsed, all attempts to revive her failed The request for the anæsthetic had been communicated to the dispensary by telephone, the dispenser took a bottle of 'Nupercaine', instead of novocain, she explained at the inquest that she had no doubt that nupercaine had been asked for "because we frequently dispense it in saline, whereas novocain is usually dispensed in distilled water" The coroner, remarking that the mistake had been frankly admitted, said he felt that the similarity in the names of the drugs was unfortunate They could easily be confused in an oral message unless enunciation was very clear

'Nupercaine' is a proprietary name for cinchocaine (B P) Formerly 'Nupercaine' was issued as 'Percaine', but this title was changed to avoid confusion with procaine

In the second case [2] a local anæsthetic was being injected into the interspinal ligaments The prescription did not specify the quantities of the adrenaline to be included with the 2% solution of novocain It had apparently been expected that the strength of the solution would be 1 in 50,000 The actual strength was 1 in 1000 A consultant pathologist told the coroner that death was due to heart-failure He had carried out considerable research to ascertain the toxic dose of adrenaline but had no definite results to give It was possible that a nervous patient might secrete adrenaline in excess The practitioner concerned said he had not specified the actual quantity on the prescription, as he thought it was a standard prescription

In both cases a verdict of death by misadventure was recorded Hospital managements will once more be reminded of the constant need of supervision, vigilance, and correct method

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[1] *Leicester Mercury* Sept 8 1953

[2] *Yorkshire Post* Sept 23 1953

In England Now

A Running Commentary by Peripatetic Correspo

NOBODY has heard of Fumaretto di Bocca di M —certainly nobody at La Spezia in whose provin are, hardly anybody at Sarzana the local town, even at Ameglia, the fairy-tale walled village perch the top of a hill at the other side of the estuary Bocca di Margra is known as the bus terminu a few have heard of Fumaretto itself

Our holiday party originally contained two peopl spoke Italian Since they left we have fallen ba French, which nobody here speaks, and School Cert Latin plus scientific terms The former rarely le down *Veni, Vidi, Vici*—good old Julius Cæsar *Gray's Anatomy* is less reliable Dura Mater s Cattivo Mama and all the anatomical fruits and have let us down Despite these tribulations we h compared all the price range of food in the two c but our final conclusion "What you gain on the sw you lose on the roundabouts" is only translatabl a rather complicated story about a man who was on Wednesday and worked hard on Saturday Ra are easier, but English diet is quite inexplicable If t don't eat pasta, can't afford wine, are not used to r and pay sixpence for an egg, what *do* they eat ? E and jam—yes—rosbif—yes—but what else—te well pouding Yes we all know the English eat very l they spoil their teeth and appetites with sweets tea, but it must be a hard life without wine

Our landlord—who has sailed the seven seas a captain's ticket—was helpful about our lan trouble, and lent me the *Master Mariner's Compan* published in Naples in 1901, which had a glossar nautical terms in six languages, so that with care l discuss the equivalents of dunnage, bill of ladin harbour master /Unfortunately only the Italian alphabetical

Everyone wanted to know what sort of do were—a woman must surely be Specialiste, C or Pediatriche We worked in the National Service, did we ? A good thing surely for poor —but what sort of job did we do ? Psychiat don't understand—oh—head doctors, yes we heard of them but we don't need them here, you s have good red wine The joke resounds from the ca to the knife-grinder, and echoes down the valle olives "The English would not need you if the our good red wine"

* * *

The position of host at a wedding party is with anxieties, not the least of which is a fearful f boding that the hired coat, fancy waistcoat, s bag trousers, and drab shell (grey top hat to wou not arrive on time or that, when they do arrive will be found to fit only a David or a Goliath was well with mine, except the drab shell which been built apparently to encase the cranium of a Gr with hydrocephalus it engulfed not merely the but also the ears, and a last-minute exchange had effected Another anxiety is whether the drink hold out, for nothing is worse for the reputation to have one's guests departing with dry lips and par throats looking earnestly at their watches to see if opening time Happily we had budgeted correctly as our delightful French friend remarked, even went home quite fed up and drunk What more one ask ?

* * *

One of the teaching-hospital registrar's duties provide examination cases when his chief is invite examine for the membership or other less distingu diplomas Five days' notice is not too long to ten suitably gross yet mobile cases at any season year, but in August even the professional patient holiday, and the evening before the current ex was two "light" With the usual dearth of ph signs in the wards, anything with a lump, limp, or wh was welcome My not overcritical choice fell on a fe house-physician who had returned to his alma with bronchial asthma brought on by devotion to elsewhere He could walk and might confident cted to wheeze So next morning after breakfast off vent with the acromegalic lady the tabetic gentle , the fibroid lung and the mitral stenotic with aortic mpetence and the cunningly kinked right carotid y which simulates an aneurysm

have often had qualms about asking patients to come caminations. I had an idea that the postcard Accept the invitation was sent back with bad grace after a t deal of grumbling, just to oblige the doctor But having had a reliable spy in their midst, I know I was wrong All were glad to answer the call and that they had a duty to the young gentlemen lents take note) who wished to qualify; for if their ases could not be cured they might at least make use of their ailments in the service of society n the lady from the distant suburbs who had to leave o at 6 A.M. had no grumbles. The regulars greeted other fondly and inquired after their acquaintances had not received or had declined the call to duty new members of the troupe were coached in their ect and warned what to expect

he highlights of my medical fifth-columnist's day his meeting with his former chief who recognised and after a perplexed greeting retired to a respectable ance and his encounter with a foreign candidate se diagnostic methods were rather oblique: 'Which ital do you come from?' followed by 'What is the e of the doctor who is treating you?' He also rted that each examiner steered the candidate ards his own specialty, the cardiologist harping on iac asthma the allergist on pollen and the neuro- t on nothing in particular The seven-and-sixpenny rarium bought us each a glass of ale

* * *

he Earles live in a cottage on the edge of my practice he depths of the country and far from a bus route nt out to vaccinate the twins When I arrived the ssed but cheerful Mrs. Earle was striving to bottle- the twins simultaneously and also to keep an eye her adventurous toddling daughter I thought aps that it might be less disturbing for them if I inated the twins while they were still feeding, and ite the toddler's well intentioned efforts to help—it one of those occasions when one would be glad of hands and six eyes—we were getting on famously l the telephone rang

rs Earle being immobilised and there being no other lt in the cottage I left her in charge of the children my small apparatus and hurried downstairs to ver the call It was the kind health visitor ringing o inform Mrs. Earle that the doctor would be calling morning to vaccinate the twins.

* * *

ne of our favourite relaxations from the strain of demic life is the study of the weekly statistics of ctious diseases. Lot of measles about we say king our head knowingly; bad year for dysentery these poor clinical chaps are having a bad summer' click our tongue over the enteric figures and speak ushed tones of the decline in scarlet fever Recently ever a new emotion has been added we have a t pride in the whooping-cough returns. Remember sharp spike a couple of weeks back? That was us ht above the maximum figures for the last ten years went just like that As the spasm shakes us in the t, and we rush our asphyxiated stomach to the n it is a consolation to know that we have made ory

nd not only that—we are learning a lot of clinical licine too Both the baker and the man who brings nd the lemonade tell us we should go round by the works every day—the smell of the gas always stops vomiting The butcher favours blowing into a le—it fixed up his partner's niece proper But fellow who really impressed us was the milkman knows somebody who got a prescription that took cough away from their kids in no time ' All you s ask the chemist for that stuff that tastes like onions old us you'll be right in a jiffy

* * *

ying of the Week.—I have no memory for faces but a derful face for memories

Letters to the Editor

CLINICAL PATTERN OF CHRONIC BRONCHITIS

SIR,—The paper by Dr Oswald and others in your issue of Sept 26 interested me greatly I wonder if it would be possible for him, now that he has his team of investigators and questionnaire ready at hand, to carry out the same inquiry in that group of patients which he has discarded as asthmatics Then he could compare these results with his figures for chronic bronchitis. He says—and I can well believe him—that ' some difficulty was experienced in determining the common usage of the term 'chronic bronchitis as opposed to asthma Surely the distinction is not a valid one though admittedly traditional

His paper goes far to confirm me in my view that in fact these two terms designate merely the clinical extremes of a single pathological entity

One visualises the same sort of relation between chronic bronchitis and cat asthma as exists between chronic eczema and, for example acute primula dermatitis Both are allergic reactions and there is an unbroken clinical gradation between the two extremes Secondary infection often complicates and aggravates the more chronic states in each but infection is not the primary cause

The survey brings out many points in which chronic bronchitis resembles the textbook features of asthma

> A relatively high incidence of allergic disorders among the relatives the frequent appearance of respiratory illness in childhood; colds, presumably in most instances vasomotor rhinitis, which " go down to the chest mucoid sputum with prolonged and *distressing morning cough conspicuous* bronchospasm and breathlessness aggravation during winter months and by a number of respiratory irritants and allergens and a high ultimate incidence of emphysema.

The presence of a very strong bee in one's bonnet almost precludes a detached and scientific approach to such a problem at any rate from a statistical angle. Dr Oswald's team would appear to be in an ideal position to tackle it, for he has already selected his asthmatics by exclusion and therefore without any bias in favour of a relation between the two conditions.

Plymouth. W A LISTER

GROUP PRACTICE

SIR,—The two articles by Dr J S Collings (July 4 and Sept 19) present a most interesting and inspiring contribution to present day thought on the development of general practice I should like however to analyse some of Dr Collings's proposals to make some criticisms and to add a few suggestions

As I understand Dr Collings's proposed scheme of basic group practice it is essentially a partnership of up to five men working in common surgery premises for their mutual aid both in consultation with one another and in order that they can help one another during temporary absence on a rota system and that they may be in a position to have more ample and suitable accommodation for their work than is available to one man alone. Also that they may be able economically to employ a sufficiently ample staff of ancillary workers to relieve the more expensively trained doctor of a great deal of his routine work This it is suggested will allow him to use his long training where it is really required

Of course all these are not new proposals What is new is concrete suggestions for putting these proposals into effect and converting vague ideas into a practical working proposition.

Dr Collings also puts forward, as a corner stone of his scheme a proposal for an appointment system of practice I should like to discuss this latter proposal first

Dr Collings suggests a system of appointments of either 15 or 20 minutes If a doctor sees patients at the surgery for a total of 20 hours a week (i e , ten 2 hour sessions, six mornings and four evenings) he will, if all appointments are always filled, deal with 60–80 surgery consultations a week—about 3600 a year For a list of 2500 patients, which is Dr Collings's suggestion, the surgery attendances will be about 1 5 per patient per year This is about half the actual urban figure at the present time Dr Collings suggests that the ratio of "nursing procedures" to doctor's attendances may be as high as 3 to 1, when the scheme is running—by which I presume he implies that on the average a patient will be seen by the doctor on only 1 of his visits in every 4 This would certainly make such an appointment system perfectly practicable, but I find it difficult to accept this ratio One would like to know if Dr Collings is assuming this figure or if he has seen it actually in operation in the urban industrial class practice He appears to visualise a practice in which several nurses are busy throughout the day dealing with "nursing procedures" for patients who were previously seen by the doctor during one of his comparatively brief consulting-hours and who will not need to see him again for several visits

But this is pure phantasy A brief analysis of the last 100 consecutive patients who attended at my surgery shows that I called on my nurse to help me with about 1 in 4, and in not more than 2 cases could she properly have dealt with the patient herself All this does not mean to say that a good nurse in attendance cannot save a vast amount of the doctor's time , but, so far as my own practice is concerned, I cannot see any work for her for long periods of the day apart from the doctor's presence, which is apparently what Dr Collings is suggesting I should like his elucidation on this point

In a description of an appointment system in a mixed general practice which was recently published, 5 minute appointments were attempted and, with some latitude, were found to be workable With ample nursing assistance, I believe 6 minutes per consultation is possible and might be very successful It does, however, rather scale down the type of leisurely, highly efficient practice suggested There are, however, two other difficulties which suggest themselves to me I think a proportion—perhaps a considerable one—of my patients would resent an appointment system Many people do not like telephoning, which in any case is not free like the doctor, and they would certainly not come to the surgery to make an appointment Nearly all "first consultations" would turn up without an appointment and would certainly resent being kept waiting while late arrivals came by appointment and were seen at once The second difficulty is that this system requires attendance at the surgery of a receptionist or appointments clerk for a very large part of each day and I feel that this would be difficult to arrange and very expensive I have come to this conclusion with great regret as I should very much like to see such a system working in my own practice

Apart from the appointment system, Dr Collings's scheme is most attractive and is an extension and elaboration of arrangements which many partnerships have worked out for themselves I feel the greatest stumbling block, as in so many aspects of the health service, is that of finance From my own experience, which covers, on a somewhat smaller scale, much of the proposed layout I am in a position to speak with some confidence on this point I agree with Dr Collings that
each partner should have a separate consulting room
that they can all work at the same time I also agree
h him that a separate small examination room is
uired to each consulting room, and preferably one or
over , 6 ft by 6 ft is large enough for these They
t be sound proof, and for that reason I prefer them
to open direct from each consulting room I also
r rather more waiting room accommodation Apart
these minor points, I am with him
cost of buying, converting, and equipping such a
at least £1700 per doctor It is only because

the older type of dwelling house in our larger t
comparatively inexpensive to buy that the figure
much higher To build new premises is prohib
well as heart breaking One great point in fav
converting the older house is that living accommod
can be provided upstairs, in converted flats, for a
keeper, and for an assistant's or locum's accommod
and this solves many problems without adding mat
to the cost But this cost is nevertheless consid
and I repeat I do not think one can count on less th
average of £1700 per partner—more for small group
a little less for large ones Dr Collings does not
the day-to day cost of running such a surgery

Rates, heat and light, telephone, repairs and ma
insurance, and cleaning may be estimated at abou
year per partner—again a little less for large grou
little more for small ones This is in addition to th
cost of capital finance If all the capital required
borrowed, the annual interest and sinking fund over
may perhaps add up to £130 per year per partner
that the annual cost of running such a central surgery
taken as upwards of £350 for each practitioner using it,
the employment of medical auxiliaries I agree wi
Collings that the optimum number of these is one per
Presumably they will cost about £350 per year each
have now arrived at the figure of upwards of £700
"partnership expenses" for each member of the group
main item under the heading of "partners
expenses" will be the car, which, with depreciation
into account, will probably be at least £450 There
further small personal expenses, and £50 should cover
The total practice expenses are now in the neighbour
£1200 per partner A list of 2500 patients will bri
about £2500 gross, and there will be a little more
wifery and some small private fees My experience
these additions, in urban industrial practice, are sm
dwindling

We find, therefore, that the man wishing to
as his inclination and professional conscience
must spend very nearly half his gross income to
this end , and if, as I agree, 2500 is the maximum
he can properly attend even in the ideal circum
of practice visualised, then his net income can
more than £1300 subject to income tax What
to the mind is, of course, not original the
payment by counting heads is absurd—it simply
premium on the type of practice castigated by
Collings in his original report and places a heavy
the competent and conscientious doctor

At this stage can any useful suggestion be
regarding this ? In my view it can 30% of the
pool is now regarded, for superannuation pur
"expenses of practice" I would suggest that
can be shown, by accountant's figures, to the sati
of an appropriate committee that the propor
expenses in any properly formed and conducted
greater than the general average, on account of
incurred to the substantial gain of their patients
they should receive an additional sum towards
expenses This would, of course, reduce the
capitation fee per head It would tend to sub
efficiency and reduce lists to a reasonable size
realises better than I do that this is a utopian sugg
and I would like to make another, more likely to
substantial measure of support

In my own partnership we have provided for
surgery premises more or less on the lines indicated
Collings For ancillary help we must perforce conte
selves with one part-time trained nurse Other
auxiliaries we must forego, but the central surgery form
seed from which I feel all improvement in general p
grows I do not agree that a group can function at all
premises to practise in It is very likely to do incre
good work if it is once formed and properly housed
necessary capital outlay on housing may suffocate it at
The building societies do not cover quite this need

If a central ad hoc committee were to be set up and
to advance from national funds the capital required

p who could satisfy a committee of the executive council the local medical committee that their proposed scheme urgeries was sound and efficient then I feel such schemes ld be widely put into effect and a great step forward to oving the status of general practice would have been n The central committee might be known as the Practice ommodation and Group Committee It might in many s resemble the present Medical Practices Committee and omposed of general practitioners and lay members who ld have among them a surveyor and a financial expert chairman should I believe be a doctor The advances would control might be loans up to say £2000 per partner a period of 20 years, at the same rate of interest as is paid he compensation money—namely $2^{3}/_{4}\%$ After all the stry have some £30 million of our money still in this fund ne surgery would slowly become the actual property of the p *and a retiring partner could sell his share to a successor* could, in his turn borrow from the fund

e scheme should commend itself to the Ministry since apital cost of providing very suitable surgery accommo n throughout the country would be less than £1 per nt attended and this is perhaps 10% of the cost of th centres which I agree with Dr Collings are quite alistic This cost would be a repayable loan

e annual charge to the partnership including some nursing would be less than 2*s* 6*d* a year in respect of each patient he list and in the experience of those of us who have had good fortune to practise from such a surgery no money ever been better spent

aving once got the surgery the group will at any rate be to use what ancillaries they can afford, and general rovement in practice will come step by step

here is one more point Many of the medical lliaries mentioned by Dr Collings are or should be, ady provided for the patient being paid by other olies of the health service This applies to nurses, th visitors, physiotherapists laboratory technicians

It might be possible to obtain their part time ices at the group premises by proper coöperation in health services where such groups are in full operation.

ne can only reiterate Dr Collings s plea for reorganisa of our work, by ourselves for the mutual benefit urselves and our patients.

oydon Surrey

Reginald N Deane

* Dr Collings s proposals for the financing of group ctices are set out in his third article which we hope ublish shortly—Ed L

LABORATORY DIAGNOSIS OF SMALLPOX

ir,—I feel that your annotation last week on the istry of Health brochure on this subject is a little mis- ing and to some extent dangerous You state e emergence of reliable laboratory tests has reduced erally the period of doubt instead of depending protracted clinical observation in a smallpox hospital an do tests which rapidly and convincingly aid the nosis, often without moving the patient Although his paragraph he refers to the medical adminis- or whoever that may be the word clinician is used equently

t must be recognised that rapidly is a relative n ; a delay of two to three days is frequent, and in a ber of instances laboratory tests may still leave the nosis in doubt A real suspicion of smallpox *must* treated as administrative smallpox and in my ion no specimen should ever be sent to a laboratory out the full knowledge of the local medical officer ealth who is responsible for taking any action he iders necessary Suspected smallpox must be treated mallpox as far as vaccination of close contacts is erned At least one avoidable tragedy occurred he recent outbreak in Yorkshire and Lancashire to waiting for the laboratory report a matter of o days before the vaccination of known close contacts suspected case.

rateful as we are to the virologists for their work his field and the inestimable value of tests properly applied we are already falling into the dangerous practice of dividing cases into suspected ' and confirmed and regarding the laboratory as the only method of confirmation We must avoid in smallpox something similar to the throat swab ' obsession which has occurred in the diagnosis of diphtheria, where the practitioner would ignore even a ' bull neck ' while he waited to obtain a positive swab

Department of Preventive Medicine and
Public Health University of Leeds

C W Dixon

POLIOMYELITIS WELSH REGIONAL BOARD AND MINISTRY OF HEALTH

Sir —We have read with some dismay a document just circulated by the Welsh Regional Hospital Board to every consultant asking them to ensure " that the arrangements for the admission and treatment of cases of poliomyelitis in their regions are up to-date and efficient, and reporting a meeting several weeks ago of thirty five physicians otolaryngologists and anæsthetists together with representatives of the Welsh Board of Health the Regional Hospital Board and a number of coöpted members, which recommended that teams should be set up throughout Wales for the treatment of acute poliomyelitis comprising a physician, E N T surgeon anæsthetist neurologist and physiotherapist

Throughout the whole of this lengthy document and its attached memoranda and reports and throughout the whole of its recommendations, there is never one single mention of the orthopædic surgeon, who of course has the responsibility of looking after these patients for the rest of their lives and cannot do it well unless he starts from the beginning

No orthopædic surgeon was invited to attend the conference There was no proposal to include an orthopædic surgeon in any of the teams—only a physiotherapist who bless her heart, would not get far among the otolaryngologists and anæsthetists who are to treat poliomyelitis. No view was sought from any orthopædic surgeon—there was only a report from Dr Ritchie Russell s medical registrar

Orthopædic surgeons who are necessarily tolerant have applauded the recent enthusiasm of some physicians and neurologists in the management of poliomyelitis, especially since the recent epidemic in Denmark which showed so high an incidence of bulbar palsy (though let it be noted, a high incidence also of limb paralysis) even when recent observations and writings have sometimes tended to suggest that only physicians or neurologists are really capable of treating acute poliomyelitis

But when enthusiasm becomes so fanatical that every consultant in one region of the Ministry of Health and *indeed in the whole of one country*—Wales—is advised that no orthopædic surgeon need be consulted on the advisory committee or appointed to any of the special teams and that a physiotherapist will suffice to aid the neurologists, otolaryngologists, and anæsthetists in the treatment of poliomyelitis, it is time to remind ourselves that when this was last done—ten or twenty years ago—we had great disasters and many horrible deformities which could have been prevented but were relieved only after years of surgical treatment

The British Orthopædic Association recognises at once the vital and imperative part that physicians, neurologists and other specialists must play in the treatment of poliomyelitis in its acute stage It knows, too that the life-long treatment of patients with residual paralysis succeeds best when orthopædic management starts early It asks only—and not for reasons of courtesy but only in the interests of good preventive treatment—that consultation and collaboration should begin from the beginning

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Reginald Watson-Jones
President,
British Orthopædic

PAIN IN CHRONIC GASTRIC ULCER

SIR,—I would be glad to clarify some of the points raised by Professor Pickering in his letter of Sept 19

(1) He rightly states that I have postulated physical and chemical factors in inflammatory pain He accepts the chemical but, for two reasons, rejects the physical In my view, these factors, artificially separated for analysis, are in reality inseparable They are interrelated, and react one upon the other Thus, a more efficient and less congested circulation in the painful area involves not only an increase in velocity and volume of flow, and a decrease in pressure, but also a more rapid clearing from the interstitial fluids of the irritating products of inflammation And vice versa, the chemical factors influence the physical—for example, by damaging capillary endothelium

(2) His first reason for rejecting tissue tension as a pain factor is as follows "I should hesitate to base a general principle on one experiment in one subject" But the evidence that tissue tension is a pain factor is based upon a multitude of experiments in a multitude of subjects They include patients with painful inflammatory diseases in whom digital pressure, and dependency and elevation of the part influence the pain, patients who are given injections, by dentists and by medical practitioners, of therapeutic and local anæsthetic agents, and who note an initial pain caused by the prick of the needle, and a second more severe pain which accompanies the injection of the fluid, and which is more marked if the tissue is inflamed, or structurally less distensible They include patients whose pain is relieved by incision of an abscess, or by trephining the nail over a hæmatoma, or the removal of a dental filling over an inflamed pulp The experiments include every systolic throb of every throbbing pain

(3) His second reason for rejecting tissue tension as a pain factor is that the quantity of tissue tension has not been measured But, even in the absence of direct measurements, we can recognise changes For example, that increased function causes increased blood-flow, even though we have no exact measurement of the increase in function, that lightning causes thunder, even though we have no measurement of the electrical discharge Although I know of no technique whereby tissue tension can be directly and exactly measured, it bears a direct relation to the height of the part relative to heart level And this can be measured and expressed in inches as a column of blood This relative height bears a relationship to rate of healing, as well as to pain Alterations in tissue tension are reflected also by the hardening and softening of the parts, and these can be appreciated by the clinical scientist, even in the absence of the instrumental methods of physical science

(4) He doubts whether compression of nerve-fibres is the actual mechanism whereby a pricking or crushing injury causes pain But the mechanism of the initial pain of pricking or crushing, and the doubts about it, are not relevant to the subject under discussion, which is pain due to inflammation

(5) He asks, 'But what events in the stomach and duodenum determine this almost predictable variation in tissue tension ?' I have described these events elsewhere at some length, with diagrams and mathematical proof, but the idea is complex and I fear that I have failed to express it adequately and clearly The 'almost predictable variation in tissue tension,' is brought about (a) by the variations in pressure and flow of blood, which accompany the change from the resting to the active state, and then from the full to the emptying state and (b) by variations in the postural tone or shape of the gastric walls These hæmodynamic and postural changes are themselves brought about by the ingestion of food, its digestion and evacuation But these changes are unequally distributed between the indurated ulcer mass and the more normal gastric wall so that the principle of the Y-tube and other hæmodynamic factors are brought into play, and influence, not only the local circulation of blood, but also the [illegible] and chemical state of the interstitial fluids, [illegible] influence pain

(6) He parts company with me here, because h that the matter is complex, and the evide "nebulous," or as I would put it, incomplete next paragraph he describes the "acid" hypothes shows that the matter is complex, and the ev incomplete If then, a choice is to be made betwe "inflammatory" and "acid" hypotheses, in ea which the matter is complex and the evidence incom I would select the "inflammatory," because the mation is always present in adequate amounts, the acid, and the inflammation has been sho fluctuate directly with the pain periods, wherea acid has been shown not to fluctuate directly the pain periods, although it frequently fluctuates i reverse manner, thus disproving the acid theor Knud Faber[1] and many others have pointed o acidity of the gastric contents becomes higher pain becomes less

Finally, I would like to say that I apprecia data on gastric function collected by Professor Pick and the worth and thoroughness of his ob even though I differ from him in their interp in regard to pain

Sydney

V J Kin

PERIODIC MEDICAL OVERHAUL

SIR,—The point of view expressed by Sir Ad Abrahams (Sept 26) seems to me to be based incomplete conception of the purpose of period overhauls, and I find his arguments unconvi

He considers, rightly, that the first function o examination is the detection of early diseas surprised that it did not reveal two cases of ver progressive malignant disease and that in a th where it revealed multiple myelomatosis this co be cured There is a stage in every disease befor diagnosis is impossible, and he might as well hav a case of smallpox appearing only a day or two a an examination Likewise, there are still many di that cannot be cured however early they are de But there are many other diseases that are silent i onset yet nevertheless can be diagnosed, and m them will benefit greatly if dealt with at that stage than left until proclaimed by symptoms

Secondly, Sir Adolphe thinks that examinatio form a basis for health education but doubts doctor is the best person to give it In this respe personal individual health education, and who b doctor can give it ?

The purpose of the periodic medical overhaul c considered under these two headings of detection o disease and health education, but I see it from a different angle Many diseases produce few symptoms in their early stages, or the sympto be wrongly attributed by the patient to age, indigestion, overwork, under exercise, or similar One might cite diabetes, hypertension, obesity, tu losis, myxœdema—in fact go through any textbo medicine and see how many descriptions of disease with 'onset insidious" How many patients at early symptoms of malignant disease to piles or or bronchitis, because they are not encouraged to doctor early ? How many women think backa normal or suffer continual fatigue without known because of anæmia from constant menorrhagia ? feet, varicose veins, corns, and a hundred and one defects go untreated because they have been tak granted for so many years A person's real s fitness cannot be assessed accurately by how he he feels

From the point of view of health education, p examinations present a powerful weapon hardly used Preventive medicine must go further than an environment perfect for the average man f

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[1] Knud Faber K Gastritis and Its Consequences. Oxford

—y widely and what suits one may kill another One y important function of periodic examinations is to the individual to adjust himself to his environment l in a few cases to adjust the environment to the man ain bad habits of living such as over-eating over iking a bad mental approach to trouble domestic ord, wearing unsuitable clothing, lack of hobbies, and ny other matters can undermine health and the lance of a doctor can help to prevent the development lisease attributable to these causes.

t is, of course wrong as Sir Adolphe says to place the phasis on the possibility of disease instead of on lth mindedness but a correctly conducted examina should place the emphasis on health and should do ch to reassure the patient

olgate Surrey ERNEST H CAPEL.

DOSAGE OF ANÆSTHETICS

IR,—In his letter last week (p 733) Dr Galley ears surprised at having achieved anæsthesia for a hysterectomy using only 8 ml of 1 in 1500 solution Nupercaine. He further states I feel quite that few anæsthetists would stake money on achiev analgesia to this height with such small doses given n average patient in the British Isles

would respectfully remind Dr Galley that should he the technique of spinal analgesia described by N C Lake[1] he could obtain anæsthesia for upper ominal surgery with only 9 ml of Light Nupercaine tion for average-sized patients As regards mid al analgesia, 5–7 ml administered by a similar nique, gives anæsthesia up to the umbilicus

inally where spinal anæsthesia is the method of ice, I use and recommend Lake's technique for high mid spinal analgesia whenever possible

ambley Park Middlesex. LOUIS CLEMENT

ROPARÆSTHESIÆ IN THE CARPAL-TUNNEL SYNDROME

R,—Dr Kremer and his colleagues in their admirable le (Sept. 19) have amply confirmed Dr M J rdle's view that the main cause of the syndrome of paræsthesiæ is compression of the median nerve in carpal tunnel Thus the controversial issue as to her the condition was primarily vascular or neural ntly settled by incriminating a pressure ischæmia e nerve

hat carpal tunnel narrowing is not the complete anation is accepted by the *Middlesex Hospital* ers for they state that in many cases the tunnel allow the passage of a raspatory Further not all of Russell Brain's syndrome suffer from the typical urnal attacks which characterise acroparæsthesiæ ccessive work with the hands, except in those cases an anatomical abnormality at the wrist appears e an invariable ætiological factor There remain wer features which still require explanation—in cular the age and sex distribution which is so ing Dr Kremer suggests that water retention may factor in precipitating the condition in pregnancy actation

ave been impressed that endocrinological disturbance lly played a part in this syndrome and have sought to ain this by fluid retention due to endocrine imbalance interesting how frequently slight ankle œdema at swelling of the fingers on waking and slight ions into the synovial spaces occur in pregnant and pausal women who suffer from this syndrome plete relief from the nocturnal attacks can frequently tained by treatment with salt restriction ammonium ide and mersalyl The fact that the acroparæs syndrome is not a symptom of the common œdematous states of cardiac and renal disease would appear to dispose of this hypothesis These conditions, however impose physical limitations which prevent the overwork that seems essential in the causation of the syndrome Fluid retention associated with endocrine imbalance may be the missing link in the pathogenesis of this interesting condition

Newmarket General Hospital R. ARDEN JONES

EXERCISE TESTS DURING HEXAMETHONIUM TREATMENT

SIR,—*Dr Ronnov-Jessen in his interesting article* last week drew attention to an unusual effect of exercise on the blood pressure of patients under the influence of hexamethonium Using this drug for the treatment of hypertension we also have found patients in whom the blood pressure falls on exercise One of us (P B S F) described this effect in a paper read to the British Cardiac Society in May of this year and a more detailed investiga tion on the variations of blood pressure during exercise and their control by hexamethonium is in the press.

In our patients who showed a fall in blood pressure on exercise, symptoms due to postural hypotension did not occur on walking if they were not present when the patients were standing still These patients were unusual in that they could not "walk off their faintness" *but their symptoms of hypotension were quickly relieved* by lying down

Charing Cross Hospital
London, W C 2.

P B S FOWLER
A GUZ

TUBERCULOSIS

SIR,—Professor Francis (Sept 26) justly takes me to task for assuming that the tubercle bacillus is ubiquitous and that tuberculosis cannot be conquered by physical eradication of the organism itself He points to the success of the campaign to eradicate tuberculosis in cattle

I am convinced. I agree that if we followed the same policy as in the case of cattle we could in time eradicate the tubercle bacillus from humans. This would mean that we would *slaughter all human infective cases* segregate in sanatoria and concentration camps &c the 30-odd million of reactors, and isolate for six months all persons coming into this country by sea or air submitting them to intradermal tuberculin tests and sending home or slaughtering the positive reactors Professor Francis I feel however would agree with me that such a policy would not be without its difficulties

I agree with him most heartily when he implies that the campaign for the eradication of bovine tuberculosis in this country is proceeding so slowly that the great majority of people do not realise that anything is happening This is only too true. He is mistaken, however when he includes me amongst this great majority In actual fact the knowledge has impinged upon my consciousness and I have referred to it in some detail elsewhere. This campaign for tubercle free herds dynastic rather than dynamic has already meandered through four reigns, and at the present rate of progress will take another thirty four years. In view of the fact that the United States succeeded in abolishing bovine tuberculosis in a period of twenty three years and Denmark in sixteen years, one can only compare the *pace* of the British campaign to that of an elderly snail with arthrodesed joints This excessively slow pace continues in spite of the brilliant work, enthusiasm and energy of the veterinary profession to whom the delay must be as exasperating as it is to public health doctors

Professor Francis accuses us of complacency because we accept the ubiquity of the tubercle bacillus in humans and points to the results of chemotherapy and B C G *vaccination but is he not confusing the eradication of* tuberculosis with the eradication of the tubercle bacillus ?

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[1] *Lancet* 1938 ii, 241

Many of the most eminent chest physicians in this country have recently expressed great uneasiness with regard to the results of treatment by the new antibiotics, and very many of them believe that the result of modern chemotherapy is to achieve a partial cure of the patient while failing in many cases to render him non-infective The seriousness of such a state of affairs cannot be exaggerated

As regards B C G vaccination, surely Professor Francis would not seriously contend that it is a method of eradicating the tubercle bacillus ! The persons to whom B C G vaccination is given do not harbour any tubercle bacilli , on the contrary B C G vaccination actually injects these organisms into their bodies in a living condition and therefore *increases* the incidence of the bacilli in the community

Professor Francis begins his letter to you, Sir, by disputing that good housing and a good standard of living would eradicate the disease , but a couple of columns of his own letter have converted him somewhat, for he ends by admitting that " the rational application of hygienic methods will lead to the eventual eradication of tubercle bacilli from large sections of the population " Quite so !

Smethwick HUGH PAUL

SIR,—With diffidence I differ from Professor Francis Undoubtedly the principle of eliminating all infectious—and all potentially infectious—animals from the herd has proved 100% successful in eradicating bovine tuberculosis I would, however, underline Professor Francis's admission that " cattle can obviously be handled much more easily than men " Furthermore, though clinically and pathologically " tuberculosis in cattle resembles tuberculosis in man as closely as any other two diseases," it is questionable whether, from the epidemiological point of view, tuberculosis in cattle is equally comparable to the " white plague " in man All the evidence suggests that, in all civilised communities in which it has been epidemic for centuries, tuberculosis —not unlike syphilis—is gradually changing in character Generally speaking, it is no longer the deadly disease it used to be 50 or even 20 years ago I believe it is generally accepted that whenever tubercle bacilli invade " virgin soil," the ravages of the disease are infinitely greater than in a population which, as a whole, has over many generations acquired a high level of immunity, and where in the course of time more and more of the most susceptible and defenceless strains have died out This slow, but steady process of relative immunisation—always interfered with by major and prolonged disasters such as war—is essentially bound up with the ubiquity of the tubercle bacillus and has been bought at a high price But whereas in 1947 the death rate in this country was still over 50 per 100,000, it has since then sharply dropped to less than half that figure I do not know how far we may regard ourselves as responsible for this statistical trend, which is not matched by a similar reduction of the incidence rate We can hardly tell how far better housing, improved food and living standards, our advanced methods of earlier diagnosis and more effective treatment, or epidemiological factors (such as the survival of the fittest after the elimination of the unfittest) or psychological and other factors not yet clearly recognised, have played, and are still playing, a part in this startling process

But so far as our efforts to control the spread and the course of tuberculosis is concerned, this is a different proposition from trying to banish from our shores a virtually ubiquitous and mostly quite harmless germ May I repeat a warning which Professor Selter of Königsberg sounded many years ago ? He predicted that if it were possible to eradicate the tubercle bacillus from our population, we should sooner or later have to fa[illegible] consequences of breeding a race completely defenceless against this infection If Robert Koch's could be fulfilled a time might come when the population of Europe and America would be as t prey to the onslaught of tubercle bacilli as ar Eskimoes or the Negroes of Africa

Meanwhile the life long isolation of all infe sufferers and possible carriers (even if we knew all) is not a practical proposition, and we must be c with such " rational applications of hygienic combined with suitable propaganda, as the mea personnel at our disposal allow Nor is Ehrlich's th *magna sterilisans* in sight So it does not look as if known rational method of prevention will in any fo able future "lead to the eventual eradicatio tubercle bacilli from large sections of the popula

Dubos and Dubos, in their excellent book quote Professor Francis, say

> " It is certain that the disease will not be eradica vaccination, and it is likely that tuberculosis will a grave problem even in unvaccinated popula economic difficulties and social disturbances interfere with general well being But if peace a hope flourishes again in the hearts of men, tuber will recede as it has always done, spontaneously life has become easier and happier And then it little difference whether vaccination, or merely bette brighter lodgings, cleaner environment and heart have been responsible for the control of tuber

Holywood Hall Hospital,
Walsingham, co Durham E G W HOFF

PREMENSTRUAL TENSION

SIR,—Mr Albert Davis (Sept 26) is right Pre tension (or, as Dr Dalton and I preferred to call paper you were kind enough to notice, the p syndrome) is not uncommon 30% to 40% of wo it in a mild form In our paper we dealt only with cases, but with no special effort Dr Dalton was collect 52 cases out of a panel of 5000 patients edly many more could be found by an search

But I cannot agree with Mr Davis about pro Has he tried it in adequate dosage ? Very few p are relieved by a dose smaller than 10 mg a day for days in each menstrual cycle, but if doses of this are administered 90% are relieved I have found not only in the relatively small series which Dr D and I described, but in a much larger series of cases omitted because my records were insuffi detailed, and later cases treated since the paper finished On the contrary, ethisterone, even in d of 50 mg a day, relieves only 65% The Mr Davis's second paragraph (in which he says that about half the patients are relieved by p makes me wonder whether he " lumped together results of the two treatments

In an experience of some hundreds of patients with ethisterone, I can only remember one who from nausea One is bound to agree that the occ disruption of menstrual irregularity is tiresome How this rarely occurs when the treatment is by intra progesterone or oral ethisterone It is a real obj to treatment by progesterone implants, convenient th these are in many respects

As we said in our paper, androgenic treatment successful, but in doses small enough to be safe virilising effects it is less often successful than p one, and it has no advantages I have not yet enough patients with methylandrostenediol to c its effects with those of progesterone or methyl terone, but I suspect that they will be equal to th the latter and therefore inferior, except in very expensive doses, to those of the former It seems slightly more reasonable to treat patients with a h natural to their sex, especially if, as both Mr Dav

spect the cause of the bother is a relative deficiency
rogesterone Dr Joan Malleson in her interesting
r published in your issue of July 15, is also of the
ion that the premenstrual syndrome is due to an
lance between the two ovarian hormones Like
Davis and myself she has had success with both
terone and testosterone though her dosage of the
er was very low and of the latter perhaps somewhat
In some cases she has had success by using an
ogen in the immediately post-menstrual fortnight
observation difficult to explain on the hypothesis
h we have advanced

ndon, W 1 RAYMOND GREENE.

PREVENTION OF POLIOMYELITIS

R,—It has been pointed out to me that in 1939
net and Lush[1] found in Melbourne that there was
elation between susceptibility to clinical poliomyelitis
absence of antibody to herpes simplex although
932 Weyer[2] had found in New York that there was
a relation In view of the well known local vari
ty of viruses there is a case for reinvestigation
I still feel that, as suggested in my letter last week,
tural history survey of the virus diseases of poliomye
patients would be well worth while

ckley Rye, Sussex. C G LEAROYD

TUBERCULOUS MENINGITIS

R,—The article last week by Dr Anderson and his
agues and your leader prompt me to send a brief
rd of the following case,

girl aged 1 year 9 months was admitted on June 11
with symptoms and signs of meningitis. Findings in the
rospinal fluid (C.S.F) confirmed the diagnosis tubercle
li were found on direct smear and by Löwenstein culture
e patient was treated with streptomycin (50 mg intra-
ally daily for five weeks followed by the same dose on
nate days for three weeks) Intramuscular streptomycin
mg daily was also given for four months
e patient was discharged on Dec 30 1949 The last
imen of C.S.F contained 45 mg protein per 100 ml.,
e blood-cells 40 per c.mm and red blood-cells 543 per
n For a year she attended the outpatient department
her condition was very good
n Oct. 10 1951 almost two years later she was readmitted
symptoms and signs of meningitis It was then learned
she had been living with her grandmother who had open
onary tuberculosis. C.S.F contained 105 mg protein
100 ml 22 mg sugar per 100 ml 674 mg chlorides per
ml and 42 cells per c.mm ; no tubercle bacilli were
or cultured. Streptomycin (intramuscularly daily for three
ths and intrathecally on alternate days for eight weeks)
p-aminosalicylic acid were given.
e patient was allowed to go home on March 3 1952 after
temperature and general condition had been normal for
a month C.S.F on Feb 25 1952 contained 85 mg
ein per 100 ml and 13 cells per c.mm
e remained well for two months and then symptoms
red. On readmission her C.S.F showed signs of active
se and tubercle bacilli were grown on Löwenstein medium.
iazid 100 mg twice daily (and no other drug) was given by
th until January 1953 (incidentally with no side-effects)
C.S.F had almost returned to normal by Sept 25 1952
tein 50 sugar 50 cells 5) During the next three months
C.S.F became normal (protein 40 sugar 57 cells 4) She
attended the outpatient department since January this
and when seen in August she was very well

he following points are worth noting (a) recurrence
r nearly two years (b) effectiveness of isoniazid
(c) absence of side-effects after prolonged treatment
200 mg of this drug daily It would be interesting
know more about the mechanism of the recurrence
tivation of submeningeal foci or reinfection)

Alfege's Hospital,
London S.E.10 E T BASSADONE.

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[1] Burnet, F M Lush D Lancet 1939, i 820
[2] Weyer E R. *Proc. Soc exp Biol., N Y* 1932 30 309

PYREXIA IN THE PUERPERIUM

SIR,—I should like to offer the following comments on the instructive and timely paper by Dr Calman and Dr Gibson (Sept 26)

The change in the definition of puerperal pyrexia as from Aug 1, 1951 (made no doubt, in all good faith to facilitate prompt isolation investigation and treatment of all infectious cases), had the immediate effect of trebling the number of cases notified each week in England and Wales Our experience suggests that this increase is made up almost entirely of cases of urinary tract infection, early mastitis (for the most part, simple engorgement of the breasts), respiratory infections and transient reactionary pyrexias which would not have fulfilled the requirement contained in the old definition which demanded that the temperature of 100·4°F should be maintained for 24 hours or recur during that period. I cannot think that an arbitrary level of pyrexia can ever provide a satisfactory basis for notification ; for example in postabortum cases it is not uncommon to encounter low grade infections, or even on occasion severe infections with spreading peritonitis, attributable to *Bacterium coli* and/or *Clostridium welchii* in which the temperature however prolonged never reaches the level of 100°F If the aim of notification is to ensure prompt isolation investigation and therapy is it any more necessary to define what is meant by puerperal pyrexia than to define what is meant by food poisoning or measles ? A common-sense deduction based on numerous factors in history and clinical findings is the final arbiter in either case If the aim of notification on the other hand, is to detect cases of true genital tract infection then the sooner the present system is abandoned the better

The bacteriological findings in the 141 cases of genital tract infection analysed by Calman and Gibson are remarkable not so much for the complete absence of hæmolytic streptococci of Lancefield group A as for the high incidence of anaerobic streptococci Routine anaerobic cultivation of all *cervical* swabs (I would emphasise the inadequacy of high vaginal swabs in seeking the true pathogen) and blood-cultures was instituted in the puerperal sepsis unit of this hospital by Prof Robert Cruickshank late in 1936 Since that time the average yearly incidence of anaerobic (both sporing and non sporing) organisms in postpartum puerperal sepsis has been 14 2% and the highest in any individual year 23 8% On the other hand, in post abortum puerperal sepsis the average yearly incidence of anaerobic organisms has been 35 4% and the highest in any individual year 57%

Our experience has suggested that organisms found on *cervical* culture in cases of genital tract infection can conveniently be divided into three groups :

(1) Those whose presence indicates active infection irrespective of the clinical findings Hæmolytic streptococci of Lancefield group A are the chief example but our experience with coagulase producing staphylococci would demand their inclusion as well.

(2) Those which though frequently harmless saprophytes are always potential pathogens, requiring only suitable conditions for proliferation—e.g traumatised tissue and necrotic retained products of conception Hæmolytic streptococci of Lancefield groups other than A, *Bact coli* enterococci and all anaerobic organisms are of this type

(3) Those organisms which are never pathogenic Coagulase-negative staphylococci and diphtheroids are the chief examples and their finding is tantamount to a negative culture

The present regrettable tendency to treat infections with antibiotics without carrying out the essential investigations is responsible for the large number of cases in which a satisfactory explanation of pyrexia is never obtained The increase in the number of available drugs and the rapidity with which organisms acquire resistance make it a matter of paramount importance that the infecting organism be identified, and its sensitivity reactions ascertained, if rational therapy is to be the rule

I notice that Calman and Gibson do not refer to the chapter on puerperal infections in *Modern Trends in Obstetrics and Gynæcology* This is probably the most comprehensive review of the subject in modern literature, and I think they might have found some useful information there

Royal Free Hospital,
North Western Branch,
London, N W 3

A MELVIN RAMSAY

SIR,—I have read with interest the article by Dr Calman and Dr Gibson but was surprised that no mention was made of a small gram-negative cocco bacillus which I have found fairly frequently in vaginal swabs from both pathological and normal cases Of the last 200 cultures from vaginal swabs taken at random, these organisms have grown in 20 instances (10%), most of these were from cases of puerperal pyrexia but some came from normal controls or cases of vaginal discharge in non-pregnant women

These organisms are best seen on the blood agar plates, after 48 hours' anaerobic culture, as minute pinpoint colonies resembling those of *Hæmophilus influenzæ* With a hand lens they can usually be found also on the aerobic blood agar plate They can be subcultured from the original anaerobic plate, and will grow aerobically on blood-agar, chocolate-agar, or serum-agar but not on plain nutrient agar The growth under anaerobic conditions is, however, always the more profuse Dr J Bamforth, investigating these organisms some years ago, found they grew well on Dorset's egg medium It is doubtful whether they are pathogenic, and as far as I am aware no one has yet given them a name, though their obvious preference for anaerobic conditions has suggested that they are related to the fusiformis (necrophorus) group, and the name "pseudo-necrophorus" has been used, but they would seem to me to be more suitably placed in the parahæmophilus group

I would be most interested to know how often Dr Calman and Dr Gibson found these organisms during their recent investigations, and what conclusions they reached about their origin and significance

Department of Pathology,
Pembury Hospital, Kent.

W M R HENDERSON

SURGICAL TREATMENT OF VARICOSE VEINS

SIR,—Various views have been expressed in your columns regarding the stripping of varices, and I entirely agree with Mr Lang Stevenson (July 25), who states that this procedure will become the standard surgical treatment of the future In most cases the entire saphenous vein can be removed through two small incisions in groin and ankle without any hæmorrhage Unlike Dr Leighton (Oct 3), I prefer to remove the vein from below upwards, since this attenuates the branches joining the main trunk and minimises bleeding The patients are able to walk within 24 hours and suffer far less discomfort than when sclerosants are used With early exercise and a careful technique the risks of deep-vein thrombosis are negligible and end results are highly satisfactory

The stripping operation, however, does not absolve the surgeon from performing a careful resection of all tributaries at the sapheno femoral junction He must also at a later date be prepared to remove or inject any [illegible] which have been missed by stripping

A film which I made of this operation last demonstrates these points, and I am glad to that such wide support is being given to this pro

Those of us who operate on many cases must join with me in deprecating the "local li technique, which makes subsequent stripping difficult but often impossible

London, W 1

R ROWDEN F

EPIDEMIC VOMITING

SIR,—Interest in your annotation last week, with the recent article by Watson,[2] prompts me this brief account

During the past three months there have in this practice some half dozen *sporadic* cases type described They have been characterised very sudden onset of vomiting without health, by the intensity of the vomiting, 12–48 hours, and by the abrupt cessation other after effect than mild prostration for a two

The following case appeared to belong to group, but had in addition definite signs of nervous system involvement

The patient, a 47 year old potter's mould mak some unsteadiness and a tendency to stumble on quickly to the loft This lasted for a week, and at work, severe headache developed and he began The vomiting continued with great severity for and then ceased The headache, which was severe over the left temporal region, lasted a few On the 2nd day of the vomiting he complained vision was blurred, and he was found to have compl sided hemianopia, with loss of pupil light reflex light was shone from the right This lasted for and then he began to recover, recovery was con the end of a week There were no other abnormal signs in the central nervous system

These cases have coincided with an epid infective hepatitis in children, and the questio identity of the infecting virus in the two occurred to me In none of these cases, howe there jaundice or palpable liver or spleen, and t pictures were quite different I have assumed that the two conditions were separate entities.

Kidsgrove Staffordshire

D G F

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1 See *Lancet*, 1953, i 858
2 Watson, G I *Practitioner*, 1953 171, 302

Public Health

Infectious Diseases in England and W

Disease	Week ended	
	5	12
Diphtheria	20	19
Dysentery	205	204
Encephalitis		
Infective	4	2
Post infectious	1	3
Food poisoning	256	244
Measles excluding rubella	802	603
Meningococcal infection	26	25
Ophthalmia neonatorum	27	41
Paratyphoid fever	11	11
Pneumonia primary or influenzal	183	169
Poliomyelitis		
Paralytic	123	92
Non paralytic	101	81
Puerperal pyrexia	246	223
Scarlet fever	483	506
Smallpox	—	—
Typhoid fever	9	6
Whooping-cough	4058	3712

*Not including late returns

Obituary

RALPH HENRY CROWLEY

M.D Lond, F R.C.P

r Ralph Crowley, whose death we announced last k, was one of the small team who in the first quarter his century planned and created our school health ice; *and it was fortunate for the service that in* e early years the post of senior medical officer at the rd of Education was occupied by someone with such rong bias towards preventive medicine

rowley was born in 1869, the son of the late Alfred wley of Croydon He was educated at Brighton Grammar School and St Oliver's Mount School Scarborough and he studied medicine at St Bartholomew's Hospital and in Berlin After qualifying in 1893 he held house-appointments at Barts and at the Hospital for Sick Children Great Ormond Street, before he joined the staff of the Bradford education authority as school medical officer He was also appointed to the staff of the Bradford Royal Infirmary Meanwhile he had taken his M.D in 1895 and his M.R.C.P three years later

[Elliott and Fry

In 1909 he joined the staff of the Board of Education, about two s after the establishment of its medical branch His agues were the late Sir George Newman the Dr Alfred Eichholz, and Dr (now Dame) Janet pbell. Before the 1907 Education (Administrative isions) Act, which placed a duty on local education orities to provide for the medical inspection of lren at school a few of the more important and ressive authorities, such as Bradford had appointed ol medical officers but for most the idea of a medical ice allied to the educational service was new wley's clinical experience and knowledge was invalu to his colleagues at the board for he was able lothe the bones of administration which in those y days was the main preoccupation of the medical ch with living tissue Sir George Newman was *inted chief medical officer of the Ministry of Health* Board of Education in 1919 and in 1925 Crowley me his *senior medical officer in charge of the medical* of the Board of Education.

lways open to new ideas, Crowley did much to ulate investigation and research both by doctors in wn department and by school medical officers working e field Investigations into the eyesight of children ropometric standards and the assessment of physical iency were some of the inquiries initiated by him and ied out by his own medical officers in collaboration those of local education authorities. Of the many mittees with which he was associated during his ial career perhaps the most important was the rdepartmental Committee on Mental Deficiency set n 1924 by the Board of Control and the Board of cation. Dame Ellen Pinsent at the former board and wley at the latter were the chief sponsors of this mittee and of the five years investigation it under-

Crowley had been uneasy in his mind for years t the certification as mental defectives under the cation Act of 1914 of large numbers of children who e merely backward educationally The committee not need much suasion to recommend that this ification should be restricted to children whose mental *ition or behaviour rendered them suitable to be* t with under the Mental Deficiency Acts but it was wley's forceful advocacy that made doctors teachers, members of the general public realise the importance his recommendation He was also chairman of the mittee of Inquiry into Problems relating to Partially sighted Children which issued its report shortly before his retirement in 1934

J E U, one of his colleagues at the Board of Education, writes:

> His vitality and enthusiasm tempered by a keen sense of what was practicable made him an inspired adviser on the development of the school medical services and on the education and well being of children handicapped by physical *and mental disabilities His sound educational philosophy* enabled him to appreciate the interdependence of medical and educational issues and assured him a sympathetic consideration of his views from his educational colleagues. Teachers felt encouraged and stimulated after his visit to a special school Even backward authorities and obdurate directors of education were overcome by his transparent sincerity and persuasive power He had an intense concern for the mental as well as the physical well being of children Child guidance and the psychological problems of the child suffering from mental ill health made a particular appeal to him. In 1920 he visited the United States to learn at first hand what was being done there for the mental welfare of school-children. He returned deeply impressed with the ideals which lay behind the child guidance service and its great possibilities for good He at once saw the medical-educational implications of this comparatively new service and threw his accustomed energy and enthusiasm into stimulating local education authorities and voluntary bodies to establish new child guidance clinics or to extend existing arrangements He probably did more than anyone to encourage the inclusion of a child guidance service in the educational programmes of this country Those of us who worked with Crowley will remember him as an inspiring leader and a man imbued with the deepest sense of humanity and idealism.

Many, as I am, writes E O L. are indebted to Crowley for opening their eyes to the importance and wide scope of social medicine

> He maintained that the doctor cannot fulfil his more specific function of treating bodily diseases, if he is indifferent to the patient's environmental conditions and his mental and moral welfare Adopting this standpoint it was not surprising that Crowley became one of the pioneers of the garden cities at Letchworth and Welwyn He was a man dominated by a passion to serve his fellow men He was a Quaker—first, last and at all times, in all things, and in all circumstances. His was the most consistent personality I have known There was *no discrepancy* between his ideals and his acts. *He would* have none of the casuistry of such maxims as the end justifies the means. Wittingly or unwittingly he was a Kantian— ought implies can, and if the end sought is right Crowley maintained that it can and must be achieved by right means
>
> He was a man with infectious enthusiasm, and in this he remained almost boyish to the end A stranger might receive the impression—a completely wrong one—that he was a man of impulse with evanescent emotions He would not give rein to his enthusiasm until he had considered carefully and critically any cause he championed *He was a great lover of* Nature and when he was moved by some fine scenery his enthusiasm became ecstasy One of my most treasured memories is a long fine summer evening we spent together in the gardens adjacent to the Portmeirion Hotel in North Wales His knowledge of flowers shrubs and trees was encyclopædic, but what made the deepest impression upon me was his delight almost childlike in its spontaneity It was fitting that Crowley when he set aside the heavy responsibilities of his post should retire to his garden It is hoped that he has left us some record of his reflections in this garden during the last fifteen years.

Dr Crowley married in 1902, Miss Muriel Priestman of Bradford and there are two daughters of the marriage

THOMAS ARCHIBALD MALLOCH

M.D McGill, F R.C.P

Archibald Malloch librarian of the New York Academy of Medicine, will be remembered by many colleagues in this country who knew him during the years he spent in Oxford and London as one of the editors of the annotated catalogue of Osler's library

He was born in 1887 at Hamilton, Ontario *one of the* three sons of Dr A. E Malloch, who was one of Lister's house-surgeons at Glasgow and a life-long friend of Sir William Osler Qualifying at McGill in 1913 he served with distinction at Depage's Belgian war hospital and later at the No 3 Canadian Hospital in France during the first world war, he took the M R C P Lond in 1919

His interests lay more in the scholarship than the practice of medicine, and his first essay in medical history, written at Osler's instigation, was the delightful book *Finch and Baines, a Seventeenth Century Friendship*, beautifully produced by the Cambridge Press in 1917, while he was serving in France His appointment in 1925 as librarian of the New York Academy of Medicine was fortunate for himself and for the academy He promoted the growth and activity of his department till it has become one of the largest and most up-to date medical libraries in the world, at the same time he made its great resources readily accessible to all serious workers He took an active part in the affairs of the library profession, and did not neglect the historical studies which were so near his heart His writings were not frequent, but they display his personal charm, while the famous rare-book collection at the New York academy owes much to his guidance In 1930 he was elected to the fellowship of the Royal College of Physicians of London, and in 1939 he was appointed FitzPatrick lecturer The outbreak of war and his own ill health prevented him from delivering the lectures, but they were published by the college in 1946 They are a learned and entertaining survey of *Medical Interchange between the British Isles and America before 1801*

He retired from his librarianship in 1949 after a coronary thrombosis He died on Sept 19 at White Plains, New York

HUGH HERCUS CAVENDISH FULLER

M D Edin

Dr H H Cavendish Fuller, chief medical officer to the Railway Executive, died at the age of 66 in St Mary's Hospital on Sept 30

He was educated at Bishop's Stortford College and at Edinburgh University, where he graduated M B in 1912 On the outbreak of war in 1914 he was attached to the Royal West Kent Regiment and he served in France with the rank of captain In 1916 he was invalided home and later he was appointed officer-in-charge of the Princess Marie Louise Military Hospital at Bermondsey

On his return to civilian life in 1917 he became medical officer of Malvern College and later he also practised privately in Malvern He was also honorary consulting surgeon to the Great Malvern Hospital and medical referee to the Ministry of Pensions for the Malvern area

In 1930 he became assistant medical officer to the Great Western Railway at its Paddington headquarters, and he was promoted to chief medical officer two years later During the late war he was in medical charge of first-aid at Paddington, and he was also medical officer to the Great Western Railway zone, to the 38th battalion of the Home Guard, and to the Kensington Sea Cadets He was vice-president of the Union Internationale des Services Médicaux des Chemins de Fer Besides his railway work he held the appointment of medical officer to the Channel Islands Airways, chief clinical assistant at the National Hospital for Diseases of the Heart, and clinical assistant at the British Red Cross Clinic for Rheumatism, Peto Place

C T N writes "Those who worked with Dr Cavendish Fuller came to admire his kindness, tact, and honesty of purpose By his services to railway medicine he has shown the way to many advances During his long illness he showed fortitude and courage, and concern for the feelings of others His loss will be deeply felt throughout the British Railways the administrations of foreign railways, and his broad circle of friends"

During his life as general practitioner, school medical officer, and in industrial medicine Cavendish Fuller made many contacts and crowds of friends outside his specialty One of them, A D W, writes

"Cavendish Fuller's desire to solve problems in an amicable way sometimes gave the impression that he was timid, but his solution was generally the best one possible and by quiet methods he generally secured his end. His good humour and his kindness of heart were unfailing, and no trouble and no distance would stop him from making a good natured gesture to a friend in trouble To the end he spared the feelings of [illegible]ound him No trace of quer [illegible] ss or awkward question revealed itself, so that one came to the
perhaps the seriousness of his illness had been conce
him The discovery of an entry in his diary man
before showed that it was he, and not his advisers,
successfully playing a part"

Dr Cavendish Fuller married Miss Janet
1917, and she survives him with one daughter

WINIFRED LINTON

S R N, Hon F C.S P

Miss Linton, head of the department for
exercises at the Brompton Hospital for Diseases
Chest, died on Sept 7 She was trained as a
St Bartholomew's Hospital, and served with the
in the Dardanelles in the first world war After
home she took up physiotherapy, and began her
the Brompton Hospital, first with J E H. Rob
later with Tudor Edwards

G M writes "Miss Linton was the most modest
regardless of women, but she was a genius. If the d
of a patient were explained to her, she would devise
and postural procedures which would reduce the dis
a minimum, and she would gain the confidence
coöperation of patients of all ages and of every rank
She trained many other physiotherapists, and
have become heads of departments in hospitals
abroad She was a woman of small stature and of no
distinction in appearance, but her zest and her
devotion to the relief of her patient carried instant
and made her respected and beloved She had a
sense of humour and she was a dear"

Appointments

BALLANTYNE, J CHALMERS, F R C S D.L.O asst.
sultant) audiology unit, Royal National Throat, N
Ear Hospital London
CAIRNS R O M B Edin D P H medical superint
medical administration of Glasgow children's hospit
CARRICK G S M B Glasg, D P H M O H and port M O,
GILMOUR I E W, M B Edin, F R C S E asst. surgeon,
General Hospital.
PLEWS W R L.R C P E, D P H deputy M O.H. and
M O Greenock.
ROBERTSON D E M.B St. And F R C.S E. asst.
surgeon Peel Hospital, Galashiels Selkirkshire
SMITH K C P M.R C.S, D P M part time psychiatri
guidance service Gloucestershire County Council.
TANNER N C. M B Brist. F R.C S part time consultant
Charing Cross Hospital London

Colonial Service

ALSTAD K S, M D Glasg M R.C.P E, D P.H
specialist, Federation of Malaya
DOS SANTOS, W A M B Camb, D Bact. pathologist, C
Trinidad and Tobago
GRECH J F M D; M O Nigeria
GRECH PAUL, M D Malta M.O Tanganyika
JACKSON J H M.B Durh M O Tanganyika
MITRA A K M B Calcutta, D P H D T.M. & H as
Aden
PENKALA, H J M B St. And M O Somaliland P
PODLEWSKI HENRYK, M B Polish School of Medic
M O Bahamas
STRISIVER E V M D Berlin F R C.S E specialist, Sk

Appointed Factory Doctors:

BALDWIN J T M.B Edin appointed factory doctor,
Midlothian
SCHOFIELD JOHN M D Manc appointed factory
Fleetwood Lancashire
YATES NORA M B Glasg appointed factory doctor
South Lanarkshire

South-Western Regional Hospital Board

ANYAEGBUNAM P A O M B N U I D L.O E N T
South Devon and East Cornwall Hospital, Plym
FREEMAN A C M A, M D Camb M R C.P senior
general medicine Exeter clinical area
MALLICK SUSHIL, B.SC L R C P E. D OBST registrar in
and gynaecology, Gloucestershire Royal Hospital, G

Births, Marriages, and Deaths

BIRTHS

ANDERSON.—On Sept 28, at Aylesbury to Audrey wi
J L Anderson—a daughter
REED.—On Sept 27 to Ralph and Freda Reed (née
M B at University College Hospital—a daughter
Mary)
RODDIE.—On Sept. 24, at Johnstone House, Royal V
Hospital Belfast, to Alix P M Roddie M B (née
wife of T Wilson Roddie M B M R C.O G—a daught
STELL.—On Oct. 2 to Eleanor Davies Jones M.B., D.
John Laidman Stell—a second daughter (Victoria

Notes and News

EDICAL FILMS AT INTERNATIONAL CONGRESS

URING the 7th International Congress of Scientific Films this year in London, 73 medical films from nineteen ons were shown Practically every aspect of medicine represented but the emphasis seemed to be on the use lm in health education and the popularisation of medical ues in different parts of the world. Films of this type ided the production and investigation of antibiotics gium) an appeal for blood-donors (Denmark) dental ene (Great Britain) nutrition (Italy) the prevention of id worm infection (Japan) the importance of vaccination eria) sex education (Sweden) anti tetanus inoculation guay) the work of a local midwife in Georgia (U.S.A.) recent advances (U.S.S.R.) Though these films were le for public distribution in their own countries, many of n were judged unsuitable for public exhibition in Great ain

f the specialised films *Manganism* (Morocco) deserves ial mention, not only because this industrial disease is arely seen in this country but because of the quality of exposition and photography Dr H Rohracher had ght from Austria a series of interesting psychological les, including a fascinating comparison of adult uniovular binovular twins filmed together while they performed lar tasks such as going up steps and shaving and rienced similar emotions as when watching a film of an operation. From Switzerland came a survey film on the of *p* aminosalicylic acid in the treatment of tuberculosis, from Germany a study of infants feeding at the breast, a bottle and with a spoon Prof J Calabek had ght from Czechoslovakia his detailed demonstration of r anaesthesia, and from France came a very complete y of rheumatism. Dr J Nauta (Netherlands) showed *excellent examples of cineradiology as did Britain's* pioneer in this field Dr Russell Reynolds. From nce also Prof A. Policard showed his new time-lapse phase rast cinemicrography film on pneumoconioses and Dr Bessis sent some electron microscope shots of normal pathological red blood-cells.

would seem that the enthusiasm for filming operations n the decline for few were submitted to this year's gress. Of the dozen medical film programmes arranged two contained films of surgical operations. In such s the interpolation of diagrams during the operation as lms from Italy and the Netherlands, makes them more ul than those which are simply visual records of operations ch as a film on a cholecystectomy which was not improved he addition of the third dimension Great Britain was, haps, more ruthless than some in selecting films to be nitted to the congress, with the result that the films wn were of a very high standard Special mention should made of *The Prevention of Cross Infection—Airborne ction* (Ministry of Health) *The Human Blood Fluke* llcome Film Unit) and *Venepuncture* and *Marrow Puncture* I Film Unit) A few examples of the scientific films during the congress were shown on a B B C television gramme Of the ten films included, four were medical n interesting reflection on the high quality of the medical s.

NEW CHESHIRE RADIOLOGY DEPARTMENT

n Oct. 2 Dr Peter Kerley president of the Faculty of liologists, opened a new and enlarged radiological artment at Clatterbridge Hospital Bebington.

he new unit is self-contained but has been planned to good circulation from the wards and direct access to the oining operating theatre suite There are three X ray ms: the general room has a 4 valve high power unit for eral and fluoroscopic work, and a cranial radiography paratus; the fluoroscopic room has a 4 valve high power for gastro intestinal chest and heart examinations; the genito urinary room has a 4 valve high power unit h urological table Electrically operated pass hatches access from each of the X ray rooms to the central kroom, and a drying room gives alternative darkroom ulation from one of the X ray rooms

he consultant staff of the department are Dr R J tting Dr J P McLaughlin, and Dr A G McCarey

University of Durham

Mr A G R Lowdon has been appointed to the chair of surgery in the Newcastle division (medical school) of the university He will also hold the post of surgeon at the Royal Victoria Infirmary Newcastle upon Tyne

Mr Lowdon is a graduate in arts and medicine of Edinburgh University He took his M.B. with honours in 1936 when he was the Ettles scholar of his year He was also awarded a Vans Dunlop scholarship in surgery and pathology He was a senior president of the Royal Medical Society After holding house appointments at the Edinburgh Royal Infirmary and the Royal Hospital for Sick Children he took the F.R.C.S.E. in 1939 On the outbreak of war he joined the R.A.M.C with a territorial commission Later with the rank of lieut -colonel he was in charge of the surgical side of a hospital in France, and in the *Edinburgh Medical Journal* he described a series of abdominal wounds treated by laparotomy On his return to civilian life he was appointed assistant surgeon to the Edinburgh Royal Infirmary and lecturer in surgery to the university He has lately published in our columns papers on the treatment of acute perforated peptic ulcer by partial gastrectomy and on the deflation of the distended bowel at operation

Royal College of Surgeons of England

Sir Ernest Finch will deliver the Thomas Vicary lecture at 5 P.M. on Thursday Oct 29 at the college Lincoln's Inn Fields London, W C 2 The title of his lecture is The Forerunner

Royal College of Physicians of Ireland

The following were successful in the D.P.M. examination held in September

L L Shenken R E Jenkins T H Bewley H M Flanagan D D Ellis, J A Kelleher

Courses for General Practitioners at Cambridge

During 1953–54 a series of one-day symposia for general practitioners will be held on Saturdays at Addenbrooke's Hospital, Cambridge Each symposium will consist of three to five lecture-discussions and demonstrations of clinical cases or modern methods

The following programme has been arranged tuberculosis and other diseases of the chest (Oct. 24) disorders of the blood (Nov 14) dermatology (Dec. 12) obstetrics and gynaecology (Jan. 9) infectious diseases (Feb. 6) cardiovascular diseases (March 6) orthopaedics treatment of injuries, and physical medicine (April 3), cancer (May 1) paediatrics (May 29) nervous diseases (June 26) diseases of the ear nose and throat, diseases of the eye (July 24) Further information may be obtained from the secretary of the Medical School Tennis Court Road, Cambridge

Medical Society for the Care of the Elderly

A meeting of this society will be held on Thursday and Friday Oct 22 and 23 at the City Hospital Nottingham Further particulars may be had from the secretary Dr H. P Jameson, 150 Harley Street, London W 1

National Marriage Guidance Council

Dr Noel Harris is to give the Gillies lecture at the rooms of the Royal Society Burlington House Piccadilly London W 1 at 6 P.M. on Wednesday Oct 28 The title of his address is Ourselves as Others See Us.

London Medical Exhibition

Lord Horder will open this exhibition at the new hall of the Royal Horticultural Society Greycoat Street S W 1 on Nov 16 at 11 30 A.M. The exhibition will be open daily from 11 A.M. to 6 30 P.M. till Nov 20

Middlesex Hospital Medical School

At this school's annual dinner on Oct 2 Mr C P Wilson the chairman was able to give a favourable account of the past year The Queen has bestowed her patronage on the hospital thus sustaining a tradition that has been uninterrupted for more than a hundred and thirty years. The Middlesex has won the inter hospitals competition for the best kept garden; the nurses have won the inter-hospitals tennis cup for the third year running (this is the second time that they have won it outright) and the students have won the inter hospitals cricket cup The Chairman spoke with awe of the high standard of the students work and looked forward to the time when they would hold a refresher course for consultants The Chairman was proposing The Hospital and Medical School and Sir Harold Boldero the dean, and Dr C. G H Newman (senior Broderip scholar) responded Sir Harold referred with pleasure to the new Institute of Clinical Research The board of governors decided that they would willingly spend much of the endowment fund on research and a house to the north of the hospital was purchased, to accommodate the institute which would be under the directorship of Prof Alan Kekwick Finally Prof B W Windeyer proposed The Chairman

Nuffield Gerontological Research Fellowships

The Foundation has awarded a professorial research fellowship in gerontology to *Dr P L Krohn, reader in* endocrinology in the University of Birmingham, and a fellowship of less senior status to Mr D A Hall, PH D, lecturer in medical biochemistry in the University of Leeds

Society of Chemical Industry

At a meeting of the microbiology group to be held on Thursday, Oct 15, at 6 15 P M at 11, Chandos Street, London, W 1, Mr E F Gale, SC D, will speak on Actions of Antibiotics in the Bacterial Cell

West End Hospital for Nervous Diseases

Clinical demonstrations will be given on Tuesdays at 5 30 P M from Oct 13 to Dec 15, in the outpatient department of this hospital (40, Marylebone Lane, W 1) All demonstrations are free, and are open to doctors and senior medical students

National Association for Mental Health

This association is holding an inter clinic conference for professional members of child guidance staffs, on Nov 21, at the Y W C A, Great Russell Street, London, W C 1 Further details can be had from the conference secretary of the association, 39, Queen Anne Street, W 1

Link between General Practitioner and Hospital

The *News Chronicle* (Oct 5) reports that at the General Hospital, Birmingham, general practitioners are to be welcomed in the wards on Tuesdays and Fridays by the registrars, house-officers, and ward sisters They will be shown the case notes of patients they recommended for admission, and told about treatment and progress.

Diary of the Week

OCT 11 TO 17

Sunday, 11th

LONDON JEWISH HOSPITAL MEDICAL SOCIETY
3 P M (Woburn House Upper Woburn Place, W C 1) Mr Albert Davis Obstetric and Gynæcological Curiosities (Presidential address)

Monday, 12th

UNIVERSITY OF LONDON
5 30 P.M. (University College Hospital Medical School, University Street, W C.1) Prof. E G D Murray (McGill) A Surmise on Some Trends in Bacteriology
POSTGRADUATE MEDICAL SCHOOL OF LONDON Ducane Road W 12
4 P M Dr W S C Copeman Treatment of Rheumatic Diseases with Cortisone and A C.T H
INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
4 30 P M (Chelsea Hospital for Women Dovehouse Street, S W 3) Mr R. H Boyd Contraception.
MEDICAL SOCIETY OF LONDON, 11, Chandos Street, W 1
8 30 P M Mr E W Riches Significance of Hæmaturia (Presidential address)

Tuesday, 13th

COLLEGE OF GENERAL PRACTITIONERS
5 45 P M (14 Black Friars Lane, E C 4) Dr G F Abercrombie Family Doctor Patient Relationship
BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P.M (London School of Hygiene and Tropical Medicine Keppel Street, W C 1) Prof R. W Russell PH D Experimental Psychopathology
ROYAL SOCIETY OF MEDICINE 1, Wimpole Street, W 1
8 P M *Section of Psychiatry* Dr E B Strauss Moral Responsibility and the Law (Presidential address)
KING'S COLLEGE HOSPITAL MEDICAL SCHOOL, Denmark Hill S E 5
5 P.M Prof E C Dodds F R.S Endocrine Background of Malignant Disease (Dorothy Platt lecture)
INSTITUTE OF DERMATOLOGY, St. John's Hospital Lisle Street W C 2
5 30 P.M Dr C O Carter Genetics in Dermatology
CHELSEA CLINICAL SOCIETY
8 30 P M (South Kensington Hotel 41, Queen's Gate Terrace, S W 7) Sir Ernest Gowers Dr Desmond Curran, Dr Eliot Slater The McNaughton Rules
MANCHESTER MEDICAL SOCIETY
8 P M (Medical School, University of Manchester) *Section of Surgery* Mr O M Duthie Retinal Detachment. (Presidential address)

Wednesday, 14th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P M. Prof A C. Frazer Normal and Defective Fat Absorption
ROYAL SOCIETY OF MEDICINE
4 30 P M *Section of Physical Medicine* Dr A C Boyle Dr Helen Dimsdale Spondylosis
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28 Portland Place W 1
Prof A. M E Sicé (Basle) Evolution of Therapeutics the Last Few Years (Bengué lecture)

College of General Practitioners

The first annual general meeting of the college hold on Nov 14 Foundation membership will meeting Further particulars may be had from the secretary of the college, 14, Black Friars Lane, Queen Street, London, E C 4

CORRIGENDA *Postprandial Attacks of Palpit Weakness after Gastric Operation*—In this article W Hamilton Smith and his colleagues (Sept 19), the "and the cells" were wrongly included at the end of paragraph in the second column on p 533

Legal Responsibility in Blood transfusion—The paragraph of Dr J D James's letter last week should " the chief problem in transfusion work is producing reactions in *recipients* who have 'reagins' plasma"

Sir Harry Platt is leaving on Oct. 24 for a two-week tour in Cyprus and Israel under the ægis of the British Coun

A party of fellows of the Royal Society of Medicine returned from a lecture tour in Northern Italy where th guests of the Lombardy region of the Italian Red Cross party consisted of Sir Gordon Gordon Taylor, Sir Cl Thomas Mr and Mrs L R. Broster, Prof and Mrs. L J Wi Hugh M Sinclair, and Mr R. T Hewitt, the secretary of the

The Association of British Chemical Manufacturers has a booklet *Marking Containers* which outlines a system of labels for hazardous chemicals. This applies primarily to in quantities exceeding 6 pints for liquids and 8 lb for so the time when the container is opened for use Copies of the *7s 6d* each, are obtainable from the association, 166, London, W 1

INSTITUTE OF DERMATOLOGY
5 30 P M Dr I Whimster Developmental Anomalies
MANCHESTER MEDICAL SOCIETY
4 30 P M *Section of Pathology* Dr R. F Jennison, Stratton Transfusion Problems.
LIVERPOOL MEDICAL INSTITUTION, 114, Mount Pleasant, L
8 P.M Prof Andrew Wilson Use and Abuse of Antib

Thursday, 15th

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P.M. (London School of Hygiene and Tropical Dr C J Popjak Biological Synthesis
ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, House, 26 Portland Place, W 1
7 30 P M Dr Norman White Retrospect
CHADWICK LECTURE
5 30 P M. (Royal Society of Arts, John Adam Street, Mr C J Regan, F R I C Air Pollution
ROYAL ARMY MEDICAL COLLEGE, Millbank S W 1
5 P M Dr W R. Bott Truants from Medicine
INSTITUTE OF CHILD HEALTH AND INSTITUTE OF NEUROL
5 30 P.M (National Hospital, Queen Square W C.1) Dr Norman Ætiological Factors of 'Congenital (kernicterus birth trauma, anoxia developmental mality)
NORTH WESTERN TUBERCULOSIS SOCIETY
5 P M (Royal Infirmary, Manchester 13) Mr F Edwards Recent Trends in Pulmonary Surgery dential address)

Friday, 16th

ROYAL COLLEGE OF PHYSICIANS, Pall Mall East S.W 1
3 P.M. Dr George Graham Value of Physiology in M (Harveian oration)
ROYAL COLLEGE OF OBSTETRICIANS AND GYNÆCOLOGISTS Queen Anne Street, W 1
2 45 P M Mr John Webster Bride Manchester Obstetrics and Gynæcology (William Meredith Fl Shaw lecture)
ROYAL SOCIETY OF MEDICINE
4 30 P.M *Section of Epidemiology and Preventive Me* Prof. H C A Lassen and Dr J R. Ibsen (C Epidemic of Poliomyelitis in Copenhagen in 1952
8 15 P M *Section of Radiology* Dr J Blair Hartley logical Methods and Values in Examination of Pa Sinus Areas (Presidential address)
POSTGRADUATE MEDICAL SCHOOL OF LONDON
12 NOON Dr Rae Gilchrist Coronary Sclerosis.
4 P.M Sir Neil Hamilton Fairley, F.R.S Schistosomiasis
GUY'S HOSPITAL MEDICAL SCHOOL, London Bridge S.E.1
5 P M Prof W Montagna (Brown University U.S.A.) lecture Growth, and Differentiation of Skin. three lectures)
FACULTY OF RADIOLOGISTS
2 15 P M. (Royal College of Surgeons, Lincoln's Inn W C 2) *Diagnosis Section.* Dr J W Pierce Manifestations of Fungous Diseases.
INSTITUTE OF DERMATOLOGY
5 30 P.M. Dr J E M Wigley Eczema

Saturday, 17th

BIOCHEMICAL SOCIETY
11 A.M (Westminster Hospital Medical School, Horseferry S W 1) Scientific Papers

CHANGE AND PERMANENCE IN EDUCATION FOR MEDICINE*

Sir Harold Himsworth
.C B M.D Lond., LL.D Glasg F.R C.P Q H P
SECRETARY TO THE MEDICAL RESEARCH COUNCIL

ERE are perhaps few things upon which all men are rood as that the problems which beset them today s in difficulty those which confronted any previous ation It is maintained that never has knowledge so complex nor the pace of life so insistent that r has it been so difficult to escape from the needs of noment and to take thought on those larger con ations which allow men to appreciate the trend of ts and the measures by which they might be con d These are comforting thoughts but they are nique To every generation contemporary problems f unsurpassed difficulty—*c'est son métier* and like very generation seeks to insure against failure by gerating this.

drag oneself away from the reassurance of present no in order to restore one's sense of perspective is ps the most arduous task which men may essay It is only on the basis of such attempts that we can e to manageable form the welter of detail which tens ever to submerge us. I take it that it is to this that the centres of thought in our civilisation—the ersities—have created occasions like the present in h they license us to step back from the canvas and y and get a broader impression of at least some of the particular picture upon which we are engaged mit at once that I have not the temerity to think lf equipped for any comprehensive consideration of ical training so let us select three problems and with them broadly They are I am afraid widely rated parts of the whole picture, so what I have to s bound to be disjointed But they have this feature mmon—each involves an essential consideration in of the major problems of medicine The first concerns ical education the second, the teaching hospital the third, professional obligation

Purpose of the Curriculum

introductory address at any medical school could ibly be considered adequate if it did not touch on the lem of the undergraduate curriculum Today it is icularly relevant Perhaps at no other time in the ry of medicine has so much concentrated effort been ted to diagnosing its ills Indeed there has just been nternational conference in London on the matter; there was no lack of controversy Let us however with something that is agreed

think that one can fairly say that every professor agreement on one point—that the course is being burdened with detail by other professors There is h truth in this and also in the further contention that *this constant preoccupation in acquiring detailed* wledge which militates against the development of student's capacity for thought. But despite this ral agreement every year sees something more added his curriculum and we seem as far as ever from overing the criterion for deciding what shall and what l not be included in the undergraduate course Now state of affairs has all the features of one of those using situations which arises when we have failed to back from the picture and answer clearly the tion What are we trying to do?

ell what are we trying to do in the undergraduate se? Are we trying to produce an Admirable Crichton who, alone in an isolated community is perfectly capable of dealing with every variety of ill to which man is heir or are we trying to give a basic education on which a man who has been taught to think can develop his special interests? Put like this the first alternative appears a *reductio ad absurdum* Yet if one examines the medical curriculum in this country it is difficult to avoid the impression that it has drifted into this absurdity The dilemma seems to me to have arisen from a failure to face the full implications of two facts First that the capacity of the human mind is limited so that men must specialise or at least have a special interest within their profession Second that general practice is as much a specialty requiring postgraduate training as any other branch of the profession

Until very recently all attempts to face the implications of these two facts foundered upon the objection that in this country a man was assumed to be competent to practise medicine independently from the moment he passed his final qualifying examination But that situation is at last changing This year the system of compulsory house appointments was introduced and now after qualification a man must have a year's practical experience before his name can be included in the Medical Register I was one of the many persons concerned in urging this requirement and one of the strongest considerations which weighed with me was that besides ensuring that the necessary modicum of experience was acquired it would free the teachers in our medical faculties from a stultifying preoccupation with practical requirements Until some such provision for postgraduate experience was made such practical requirements imposed an *insuperable obstacle to reform* of the undergraduate curriculum But the way is now clearing Undergraduate medical education provided it is remembered that general practice is also a specialty need no longer aim at producing ready made Admirable Crichtons Like any other faculty in the university the medical can now devise a course of education based on representative rather than comprehensive experience Only thus can it be liberated to become educative in the true sense that of equipping men to educate themselves

But *this reform depends upon confidence* that the appointments held in the first year after graduation are such as will adequately supplement the training given in the undergraduate period It will therefore be necessary to ensure that the nature of these appointments and the arrangements for continuing training in the hospitals where they are held, are suitable for this purpose We might well be able to learn some useful lessons from American experience in this respect

Purpose of the Teaching Hospital

Now one of the difficulties in the organisation of medical training—at least in the clinical years—is that it has to be adjusted to the structure of the health services whose facilities it requires That brings me to my second point the place of the teaching hospital in the health services of this country

Few of us would cavil at the statement that the teaching hospitals of the country are *national* assets but I wonder if the implications of this statement have been fully realised The National Health Service Act lays on the boards of governors the duty of providing the *facilities necessary for medical education and research* but does not specify the priority that should be accorded to this among their other manifold responsibilities That there is some divergence of opinion on this point is evident It may therefore interest you to know the view of one of the greatest and most successful administrators of a teaching hospital, Dr Nathaniel Faxon of the Massachusetts General Hospital in Boston He epitomised

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ddress at the opening of the session 1953-54 at the Faculty of Medicine University of Birmingham, on Oct 3 his considered judgment on this matter in one sentence

> "The functions of a teaching hospital are first, to advance knowledge, second, to set an example of practice, and third, to train future doctors, they are not primarily to cater for local needs"

Stated in this forthright manner these opinions may seem a little startling, but, if one examines them, their inescapable logic impresses

Leaving aside, for the moment, the order of priorities he assigns to these different functions of a teaching hospital, I think that we should all agree that to advance knowledge, to set an example of practice, and to train doctors are, each and all, duties which a teaching hospital must undertake But none of them can be discharged in any high degree without special facilities special staff, and specially directed effort on the part of all concerned For medical education all are required Taken together, their demands on an institution are so exacting that they are unlikely to be met unless their full realisation is taken as the primary and deliberate aim of policy to which other claims must be regarded as secondary

But let us return to the first part of this statement and examine the priorities accorded to the different functions of the teaching hospital There is the same clear logic in the sequence given to these priorities How can one set a high example of practice if one is not advancing knowledge? How can one train future doctors if one is not setting such an example? The motive point is research Personally, I would go so far as to say that in the association of research with teaching we have the essence of the distinction between education and training And it must necessarily be so if the aim of education is to liberate a man to think for himself The crucial test of a man's understanding of a subject is his ability to advance it If a student does not see his teachers thinking effectively how can he learn to think for himself? It is only by living and working in an atmosphere imbued with the thirst for new knowledge that a student can acquire that critical receptivity and perception on which alone he can rely when, as so often happens in medicine, established knowledge fails him

Professional Obligations

And now I come to my third point—the professional obligations of medicine in a changing society

This is a large and complicated subject, but as in all such subjects the underlying principles are relatively simple They are simple because they are based upon permanent features of human society And they apply, not only to medicine, but to those other human activities which, in popular opinion, are distinguished as the professions If, therefore, we are to steer our way with confidence through the detailed perplexities of the present we must endeavour to grasp clearly the nature and significance of those principles which underly the concept of a profession

The idea of a profession is entirely a social concept Apart from society it has no meaning Essentially the concept implies the recognition by society that, if its needs are to be met in a particular respect, then the body of men undertaking this obligation must be given certain special considerations In effect a tacit social contract is implied obligation on the part of the professional man to use his best endeavours to meet the particular need of his society, obligation on the part of the society to accord to the professional man such status, authority, and privilege as shall be required for him to discharge his obligations Only in so far, and for so long, as this implicit contract is observed will the profession in question survive It is as well to be clear on this point, for it is the inherent weakness of all associations of men to t the bonds which unite them together into a ne and to forget the mundane and utilitarian requirements upon which their profession depends for its continued existence

But, if professions arise, and exist, to meet a society, what is it that society requires of them

First, it requires a special competence—the skill to meet, to an ever increasing extent, t called the particular profession into existence Law that requires competence in applying and preting the rules of conduct in the particular in the teaching profession it requires the acquis knowledge and the skill to impart it, in med implies competence to preserve health and to treat Unless society has the requisite degree of confid the technical competence of its professions th helpless And what is that degree? In the pre the standard of competence required to elicit confidence is never the ordinary The needs to b are too vital for confidence to survive the suspic the best has not been available It is this which the continued prosecution of research an essential in maintaining public confidence in our profess is this which makes the continued striving after lence, rather than mere competence, the professional endeavour

But all this might apply to any skilled human It is not this which has distinguished the profe the mind of the man in the street The efficient di of our technical obligations—essential though could never have won for us the trust—and I might still say the affection—with which the regards our own profession To find the explana this we must look deeper

The whole trend of human development is tow elaboration of closely integrated communities within the structure of such can men find that which permits them to develop those special ski obtain, for the community as a whole, a master natural environment far greater than could achieved by any individual living independently each step towards individual specialisation men more dependent upon, and subject to, and we are all, unfortunately, only too well men are essentially individualistic, each with desires, needs, and interest In this conflict individual and social interest lies the dilemma society To meet it men have created, and en systems, but, although these may suffice to giv modicum of confidence required to prevent soci integration, they cannot promote that increase upon which the development of society depends can come only from voluntary acts which confidence between men, and there is no more stimulus to this than that of a man, or a body voluntarily subordinating themselves to a stand social morality more exacting than that required community in general Such voluntary subordi is the hallmark of those vocations which are distinguished as the professions It is this which a for the special respect in which they are held privileges which they are accorded

More than two thousand years ago a code of c was laid down for the medical profession To th that the spirit of this code has been faithfully o by succeeding generations of medical men we attribute the public trust which we have inherited the original code was concerned only with the re of medical men to individuals under their care. medicine has acquired extensive relations with soc general Nevertheless the spirit of the Hippocrat is as relevant to medicine now as it was two th years ago And what is its essence? It can be one sentence *Act always so as to increase trust* the first and paramount law of social ethics. In relationship with individuals act so as to increase n your professional skill and your character as a In your research act so as to increase confidence in fic integrity In public relations act so as to se the confidence of society in your profession that criterion as a guide, whatever changes occur social context neither the individual nor his sion need fear the future

ION-EXCHANGE RESINS IN THE TREATMENT OF ANURIA

B M Evans
B.Sc Lond

M D Milne
Manch., M.R.C.P

N C Hughes Jones
M A B.M Oxfd

H Yellowlees
M.A , B.M Oxfd

the Postgraduate Medical School of London and the Middlesex Hospital London

: prognosis of cases of anuria or of severe oliguria acute tubular necrosis has greatly improved since itroduction of the conservative régimes of Borst and Bull et al (1949) Previously such cases were fatal either from pulmonary œdema due to the istration of large intravenous infusions or from c arrest due to hyperkalæmia Pulmonary œdema cause of death has been virtually eliminated by n methods of therapy but cardiac arrest from kalæmia although delayed is still not unusual otassium levels in the plasma and extracellular ave been satisfactorily reduced by dialysis methods, ling the artificial kidney (Kolff 1947) peritoneal tion (Fine et al 1946) and intestinal perfusion f 1948) These methods have recently been reviewed acLean (1952) they have the disadvantages that l experience and apparatus are necessary the enance of the fluid balance is often difficult and ion may easily take place in the former two methods inal perfusion is relatively less effective and has cal difficulties, unless an isolated loop of the bowel pared surgically, but this is a severe operation for a ly ill patient.

much simpler but still effective method has been ibed by Elkinton et al (1950) who administered a xylic ion-exchange resin charged with ammonium oth orally and by retention enemata and obtained y satisfactory exchange for potassium ions, with nite fall of the serum potassium level

consider that a sulphonic resin charged with m has considerable theoretical advantages, because inge with this type of resin is more rapid, and m is more innocuous than ammonia in anuric nts. The ammonia is converted to urea in the liver vill therefore raise the already high blood urea level ldition acidosis which is almost invariable in these nts, is increased because a basic ion is exchanged ect for neutral urea Further evidence will be given that there is already present in the colonic contents many uræmic patients a high concentration of onia which will tend to diminish exchange with an onium resin. The small amount of sodium given up sodium resin is relatively harmless and does not ar to cause either œdema or hypertension A short t of a single patient treated with this type of resin een given by Bull (1952)

o describe here our experience with a sodium sul lc resin* in the treatment of five cases of anuria or re oliguria complicated by hyperkalæmia together relevant observations of the effect of the resin in a nal person on a low-electrolyte diet. All the cases of ia were from other hospitals, and therefore resin treatment was not given in some cases as early as we recommend in this paper

Methods

The resin used was of coarse grade and consisted of irregular particles of diameter 100–400 μ. The binding capacity of the resin was 3·4 m eq cation per g of resin. About 90% of this was sodium but 3% calcium and 7% ammonium ion was also present Since the resin was completely free from potassium the small proportion of cation other than sodium was of little if any importance It was administered both by mouth and by retention enema the dosage being 15 g three or four times daily by mouth and 30 g daily by enema. The resin was too coarse to be given by the narrow 'Polythene' intragastric tubes used for the administration of the fluid electrolyte free diet of Bull et al (1949) It had to be swallowed by the patient either with water or after being made into a paste with 'Golden Syrup' A resin of finer grade would be more easily given to uncoöperative patients but was not available at the time of this trial † The retention enemata were made up according to the following prescription and were easily given with the aid of a little pressure

Sodium sulphonic resin	30 g
Emulsion promulsin ‡	100 ml
Aqua dest	100 ml.

The cation content of the resin was estimated by washing out the resin from fæces with distilled water and elution of electrolytes with 2N HCl as described by Barker and Mackay (1951) Preliminary drying of the fæces was found to be unnecessary but the recovered resin was thoroughly dried in an oven at 103°C The more standard burning technique at 400–600°C was difficult with this type of resin since ashing was incomplete at temperatures below which cation may be lost by volatilisation The elution technique would be impossible if a fine grade resin were used Slightly less cation was recovered from resin after exchange in the gut This is due to the fact that divalent cations and potassium have a higher affinity for resin than sodium and were therefore eluted for analysis less completely Values for potassium exchange are therefore slightly underestimated throughout The following analytical methods were used: sodium and potassium flame photometer calcium method of Clark and Collip (1925); ammonia, nesslerisation magnesium method of Kunkel et al (1947)

During the administration of the resin the patients were given the diet of Bull et al (1949) which consists of 400 g of glucose and 100 ml of peanut-or olive oil made up to 1 litre with distilled water gum acacia being used to emulsify the oil If vomiting or diarrhœa became troublesome, the oil was reduced to 25 ml. If these symptoms persisted the intravenous régime of Bull (1952) was used This consists of the slow intravenous infusion of 1 litre of 40% glucose into the superior vena cava through a polythene tube introduced via an antecubital vein, nothing except small amounts of water being given by mouth Infusion into a large vein is necessary since this concentration of glucose rapidly causes thrombosis in smaller veins

In the normal person a modified Borst (1948) diet was used consisting of sucrose 150 g custard powder 100 g 'Casilan' 50 g (calcium caseinate) and butter 50 g made into a thin custard with 1500 ml of distilled water This diet contains only 7·5 m eq of potassium a day

Case records

Case 1.—This patient was transferred to Hammersmith Hospital on the fifth day of the oliguria She had been well until the thirty sixth week of her eleventh pregnancy when she developed severe abdominal pain and vaginal hæmorrhage She was delivered of a stillborn child, and the placenta had a large retroperitoneal clot typical of concealed accidental hæmorrhage Severe oliguria followed only a few ml of bloodstained urine being passed each day

Treatment—The patient was treated with the intragastric drip method for eleven days and then with the intravenous régime for a further nine days. The urine volume slowly increased to 600 ml daily but no more By the twelfth day of

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nufactured by Bayer Products Ltd. This resin should not e confused with 'Katonium' resin which is charged with a ixture of 75% ammonium ion and 25% potassium and would e contra indicated in anuria.

† It is understood from the manufacturers that a fine grade and more highly purified form of the resin, with the proprietary name of 'Resonium-A' will shortly be available in adequate quantity

‡ Manufactured by Watford Chemical Company

the oliguria the serum potassium level had risen to 6 m eq per litre, and treatment with resin was started In five days the serum potassium level had fallen to 4 4 m eq per litre, 270 m eq of potassium having been eliminated by the resin and only 37 m eq in the urine The blood urea level slowly rose to 430 mg per 100 ml, and the patient died in coma on the 23rd day of the puerperium

Necropsy showed gross bilateral renal cortical necrosis (fig 1) recovery being impossible owing to the widespread and irreversible renal damage

Case 2.—This patient was transferred to Hammersmith Hospital on the fifth day of the oliguria She had a retained placenta after the delivery of her first child Manual removal caused considerable shock and hæmorrhage, which was treated by infusion of dextran Subsequent cross matching of blood was thereby made difficult, and at a later blood transfusion incompatible blood was given

Treatment—The patient was being treated with potassium citrate for a urinary infection, and this was continued for some time before it was recognised that she was oliguric This caused a serum potassium level of 8 m eq per litre on the fifth day The patient was treated with the intragastric régime throughout the oliguria and with resins between the fifth and eighth days The serum potassium level was reduced to 4 5 m eq per litre after three days' treatment with resin, 103 m eq of potassium being removed by the resin and 26 m eq in the urine On the eighth day the patient had a satisfactory diuresis, and she made an uninterrupted recovery

Resin therapy would have been unnecessary in this case if potassium citrate had not been used to alkalinise the urine Sodium citrate or bicarbonate is a much safer therapeutic agent for this purpose in any condition where there is danger of the development of anuria or oliguria

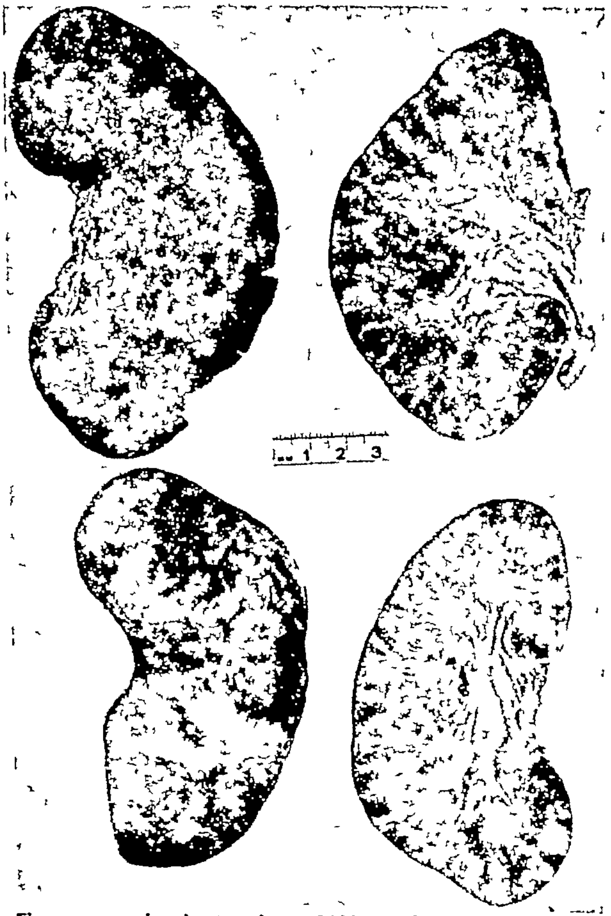

Fig - 1 and cut surfaces of kidneys of case 1, showing renal cortical necrosis

TABLE I—EFFECT OF RESIN THERAPY ON
LEVELS

Subject	Duration of resin therapy	Serum potassium level (m eq per litre)		Total of potassium removed by resin (m.eq)	P pr
		Before therapy	After therapy		
Case 1	5 days	6 0	4 3	270	[illegible]
Case 2	3 days	8 0	4 5	103	[illegible]
Case 3	6 days	8 2	4 9	280	[illegible]
Case 4	18 hours	9 2	—	7	[illegible]
Case 5	3 days	6 3	3 7	91	[illegible]
Normal person	4 days	4 4	3 3	84	[illegible]

Case 3—This patient was treated throughout at Middlesex Hospital She was a previously healthy gi 17, who had had a sudden and unexplained anuria.

Treatment—She was treated by intragastric drip eleventh day, when vomiting became so troublesome was discontinued and the intravenous régime was On the twelfth day the serum potassium level h 8 2 m eq per litre Treatment with resin reduced 4 9 m eq per litre within five days, 280 m eq of being removed Her blood urea level had been 12 100 ml on the third day of the anuria and had risen mg per 100 ml by the sixteenth day, when she sta pass small amounts of urine A satisfactory diures occur until the 21st day of the oliguria, when the blo level had risen to 510 mg per 100 ml, although the potassium level remained below 5 m eq per litre. made an uninterrupted recovery

Death from hyperkalæmia would almost have occurred had active steps not been taken to the serum potassium level

Case 4—This patient was seen and treated at hospital and was never fit for transfer He was a healthy young adult male who sustained a severe injury of both thighs His urinary output was sa for the first three days after the accident, but after th was severe oliguria On the fifth day the blood urea 294 mg per 100 ml and the serum potassium level 9 per litre

Treatment was given by the intragastric drip, but treatment was not started until the seventh day Th died eighteen hours after the first dose of resin, there been no improvement in his condition

At necropsy the resin was found to have been within the stomach and in this site to have taken 7 0 m eq of potassium A severe crushing injury of th muscles and the changes of acute tubular necrosis kidneys were found

Resin treatment should have been given several earlier, in the grave condition of the patient whe seen dialysis methods would have been preferable facilities were not available locally and the patient unfit for transfer This case illustrates how very the serum potassium level may rise in the crush owing to release from damaged muscle

Case 5—This patient was transferred to Hamm Hospital on the third day of anuria He was admitted acute suppurative parotitis and anuria of two days' He had previously had relapsing pneumonia and coccal infections associated with leucopenia, but o occasion there was adequate polymorph leucocytosis considered that the anuria was almost certainly on chronic uræmia since the blood urea level was ver being 440 mg per 100 ml, there was severe acidos plasma bicarbonate level being 9 0 m eq per litre, and was a normochromic anæmia with hæmoglobin 7 0 g pe

Treatment—Since there was no previous history of renal disease, the patient was treated as a case of anuria, the intravenous régime being used in view parotitis The latter was treated by incision and terra by mouth since that was the only antibiotic to wh causal staphylococcus was sensitive The plasma level was 6 3 m.eq per litre and three days' treatme resin was given, which reduced the level to 3 7 m.eq 91 m eq of potassium having been removed The b to 584 mg per 100 ml., and the patient died in coma inth day of the anuria

sy showed that there was severe secondary amyloid e liver spleen adrenal cortex, and a single horseshoe The renal disease was clearly severe and irreversible as recovered at necropsy from all the anatomical of the gastro-intestinal tract except the ileum The lk of the resin was however retained in the stomach g partial ileus

Results

in the patients with anuria and in the normal there was considerable exchange of sodium ion assium ammonium calcium and, occasionally, um ion The serum potassium levels fell in all the (table I) In cases 2 and 3 a satisfactory diuresis ace soon after the fall of the serum potassium d the patients made a good recovery In cases 1 although the serum potassium level dropped orily there was progressive retention of nitrogen h patients died in coma Necropsy showed that l damage, due to cortical necrosis and amyloidosis vely was severe and irreversible. Case 4 was too late since the serum potassium level was q per litre when therapy was started Death

—ANALYSIS OF CATION COMBINED WITH 1 G OF RESIN (M.EQ PER G)

	Na	K	NH₄	Ca	Mg
administered	3·01	—	0·[illegible]8	0·12	—
erson					
mal diet	0·39	0·00	0·23	0·71	1·20
rst diet	1·80	0·50	0·57	0·55	—
etention of enema for 3 hr	2·80	0·11	0·25	0·23	—
etention of enema for 9 hr	2·50	0·30	0·18	0·36	0·03
etention of enema for 18 hr	2·18	0·39	0·22	0·66	0·15
fecal resin	1·25	1·19	0·36	0·31	0·11
ecal resin	1·[illegible]0	0·77	0·54	0·38	—
fecal resin	0·44	1·20	1·21	0·09	—
astric resin	1·03	0·10	0·28	0·20	—
fecal resin	1·46	0·81	0·50	0·30	—
l necropsy specimens of rom :					
ach	1·78	0·17	0·84	0·10	—
num	0·97	0·41	1·66	0·07	—
colon	1·[illegible]	0·42	1·32	0·12	—
s. colon	0·70	0·48	0·98	0·17	—
. colon	0·54	0·67	1·25	0·20	—

ace within eighteen hours of resin being given necropsy almost all the resin was found in the h and very little potassium had been taken up late stage the patient should have been treated ysis but if resin had been administered earlier ly such a dangerous hyperkalæmia would have prevented In the normal person the serum um levels fell in two days from 4·4 to 3·3 m eq but did not drop any further although progressive um depletion continued

e II and figs. 2 and 3 present the results of analyses ns combined with resin obtained from the patients e normal person On a normal diet calcium and um are taken up in preference to univalent On the modified Borst diet containing 30 m eq um a day, considerable quantities of calcium were ged When resin is given by retention enema take of potassium increases with the period of on The comparatively long periods for which it is ry to retain the enemata before significant ge takes place diminishes the efficiency of this f administration in ill patients. Even when the was retained for eighteen hours the uptake of um was less than when resin is given by mouth he patients exchange for potassium was greater ably because they were on an electrolyte free d therefore there was less competition with divalent In most cases, however there was considerable of ammonium ion as well as potassium nia produced by bacterial breakdown of urea, is t in high concentration in the intestinal contents mic patients Fortunately potassium is taken up

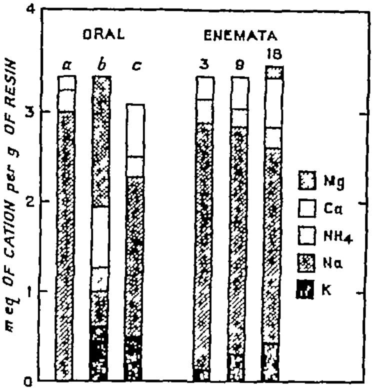

Fig. 2—Normal person. Cation combined with resin and expressed as m.eq per g : a as administered ; b recovered from fæces (normal diet) ; c recovered from fæces (Borst diet) ; 3 9 and 18 after retention of enemata for 3 9 and 18 hours respectively

preferentially to ammonium ion by exchange resins Ammonia formation proceeds in fæces after they have been discharged from the body Since stools are usually alkaline the ammonia escapes but becomes fixed to resin if this is present Thus an uptake of 0·80 m eq of ammonium ion per g of resin was found on incubation of the resin with excess of normal fæces for twenty four hours This was increased to 1·20 m eq per g if 1% urea had been previously added

In case 5 resin was recovered at necropsy from the contents of the stomach jejunum and the various anatomical divisions of the colon. No resin was obtained from the ileal contents. It was found that potassium uptake had increased progressively as the resin passed down the gut All the specimens contained considerable amounts of ammonium ion but there was no free acid in the stomach of this patient and presumably bacterial action extended to a higher level of the gastro intestinal tract than is usual

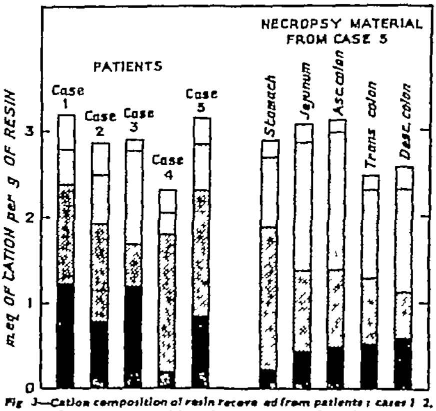

Fig 3—Cation composition of resin recovered from patients ; cases 1 2, 3, and 5 average composition of resin recovered from fæces in life ; case 4 resin recovered from stomach at necropsy Necropsy material from case 5 shows the composition of resin obtained from the various parts of the gastro-intestinal tract.

Discussion

An increase in the level of extracellular and plasma potassium to about 10 m eq per litre may cause death from cardiac arrest (Finch et al 1946) In anuria a rising plasma potassium level results from endogenous protein metabolism, with consequent transfer of potassium from the intracellular to the extracellular phase Gamble (1951) has shown that the average endogenous consumption of protein during a period of fasting is 70 g a day When 100 g of glucose is given each day this is reduced to 40 g, but no further decrease results from a greater carbohydrate intake It can therefore be assumed that anuric patients have an endogenous protein breakdown of at least 40 g a day In many cases this is considerably greater owing to fever, involution of the uterus in postpartum patients, and removal of damaged tissue, as in the crush syndrome This endogenous metabolism leads to a total increment of non protein nitrogen of at least 6 4 g a day If the average total volume of the body-water is 49 litres, this corresponds to an expected minimal daily increase of the blood-urea level of 28 mg per 100 ml Since 1 g of protein nitrogen is equivalent to 2 7 m eq of potassium (Reifenstein et al 1945), there is simultaneously a release of 17 m eq of potassium from the tissues into the extracellular compartment

The carbohydrate in Bull's régime amounts to 400 g daily Although an intake of more than 100 g of carbohydrate a day does not cause any greater protein sparing, it does reduce potassium levels in the extracellular fluid by increasing glycogen synthesis, which is accompanied by transfer of potassium into the body cells (Fenn 1940) Only the glycerol fraction of fat is effective in this respect, and there seems to be no theoretical reason for giving 100 ml of oil if it causes any nausea or other symptoms of gastro intestinal upset We therefore do not hesitate to reduce the oil intake to 25 ml a day if there are any such symptoms This amount of fat is included since it produces an opaque white emulsion which conceals from the patient that his strained vomit is being added to the intragastric drip as the most satisfactory method of restoring electrolyte loss

The resin by the oral route has been found to exchange 0 5–1 2 m eq of potassium per g, corresponding to a total of 20–75 m eq a day at the dosage of resin suggested This is usually considerably more than the daily accumulation in the extracellular compartment, and therefore, as in all the patients except case 4, there was a progressive reduction of plasma-potassium level. It has been shown (fig 3) that potassium uptake continues throughout the gastro intestinal tract, and that the exchange in the stomach is small It follows that there must be a short latent period before much effect is produced This may be further prolonged in gravely ill patients because there may be a partial ileus in some cases of anuria, with accumulation of resin in the stomach, as seen in cases 4 and 5 The administration of resin by rectum is far less effective, but is still of value if the enema can be retained long enough Where the plasma-potassium level is already greatly increased when the patient is first seen, it is preferable to give the resin by both routes Further uptake of potassium by resin administered by enema can hardly be expected after the first oral dose has reached the rectum An oral carmine marker is a useful indication of this Further exchange of potassium will occur as long as resin is passing through the gut, and may be expected to continue for about two days after the last oral dose We recommend that resin should be given as soon as the serum potassium level rises above 6 m eq per litre The effect should be controlled by daily estimations of serum potassium level, and the resin should be discontinued as soon as the value falls below 5 m eq per litre If it is stopped at this level, t [illegible] danger of serious hypokalæmia The observations on the normal person show that the serum level is rapidly reduced by the resin to about 35 per litre, and continued administration is still in removing potassium without causing any reduction in the serum-potassium level At this of depletion serum potassium levels are maintained low normal value from intracellular reserves and to be any guide to the magnitude of potassium

In some of the anuric patients the resin sodium in exchange for a considerable ammonium ion The highest ammonium values obtained from stools of case 3 and from the gut obtained at necropsy from case 5 In both of was probably some increase due to post mortem tion of ammonia, since in case 3 the stools had kept for a few days before analysis, and in case intestinal contents were not obtained until hours after death Considerable uptake of ion was found, however, in some stools analysed diately after defæcation A high ammonia stools from uræmic patients has been reported by and Dick (1933), it is derived from bacterial position of urea present in high concentration intestinal contents Resin treatment probably the amounts of ammonia eliminated, since reab this cation is prevented The amount of nitrogen by this means is small, and was always considerabl than 1 g a day Its main importance in resin is not therefore a significant increase of nitrogen e tion but rather an undesirable reduction of pot exchange by cation competition

The diets used in the treatment of anuria virtually no fæcal residue In the balance on the normal person the average daily weight of was exactly three times that of the resin ingested the same period The resin increases in weight and a half times when thoroughly moistened and is allowed to drain off It therefore follows th fæces consisted of little other than moistened res intestinal mucus There was never any tend fæcal impaction or any difficulty in evacuation stools, but it was *considered* safer to give a small wash if a bowel movement had not taken place previous two days It is essential to use small of fluid, since colonic absorption of water takes may easily lead to water intoxication

Scheme for Treating Anuria with Resins

Diet

The patient is treated as a routine with the gastric drip régime of Bull et al (1949) This of the daily ingestion of an emulsion of 100 ml of oil in 1 litre of 40% glucose If the patient small quantities of urine, the same volume of extra is added to the drip the next day If there gastro intestinal symptoms the amount of fat is diately reduced to 25 ml daily, since the extra provided by the excess fat neither diminish end protein metabolism nor favour synthesis of gl The patient's vomit is strained and added to the the most satisfactory method of preserving elec balance If vomiting or other gastro intestinal sym persist the intragastric drip is discontinued, intravenous drip of 1 litre of 40% glucose a day through a polythene catheter passed via an ante vein into the superior vena cava Only small water equivalent to the preceding day's urine are given by mouth

Control of Infection

Scrupulous attention is paid to oral hygiene muscular penicillin 1 mega unit is given daily

Biochemical Control

After a preliminary assessment of the levels of potassium, chloride, bicarbonate, glucose, and urea

treatment is controlled by daily determinations
ssium urea and glucose Resin treatment is
as soon as the serum potassium level rises above
per litre and is discontinued when it falls below
per litre The resin is given orally at a dosage of
ree or four times daily Daily retention enemata
ing 30 g of resin are given following a small
rash Enemata are discontinued as soon as oral
belled with an oral carmine marker given with the
se is evacuated If the plasma potassium level
ove 9 m.eq per litre despite resin therapy, arrange
are made to treat by dialysis either peritoneal
or the artificial kidney being suitable for combina
th resin treatment This will be extremely rare
of the large amount of potassium removed by
n but may conceivably occur in cases where there
n considerable tissue damage, as in severe burns
uria and in the crush syndrome
opriate amounts of soluble insulin are given by
n twice or three times daily if the blood-sugar
ses above 200 mg per 100 ml Many patients
a high blood-sugar level on these dietary régimes
appears logical to favour glycogen synthesis and
ient transfer of potassium into the cells by
ous insulin

a

nsfusion of packed cells is given if the hæmoglobin
han 70% on the Haldane scale

COMMENT

suggested régime differs from that of Bull (1952)
that every effort is made to avoid potassium
by the *early* use of resin, that less insistence is
a high fat régime for the reasons discussed above,
it insulin is used routinely if there is any tendency
erglycæmia.

Summary

treatment with a sodium sulphonic ion-exchange
five cases of anuria or severe oliguria complicated
perkalæmia is reported. The serum potassium
as satisfactorily reduced in four of the patients,
nal recovery in two

patients died from severe irreversible renal
and one from hyperkalæmia before the resin
xert any significant effect

resin is more effective in removing potassium when
by mouth than when it is given by retention

resin continues to take up potassium in exchange
lium throughout its passage through the gastro
al tract. The effect is therefore delayed after
t dose and prolonged after the last one.
heme of routine treatment with ion-exchange
is given for anuria and severe oliguria

hanks are due to Bayer Products Ltd. for the sodium
ic ion-exchange resin, and to the various physicians,
s, and obstetricians who made their patients available
trial.

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EPIDEMIC BRONCHITIS IN CHILDREN

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Epidemics of bronchitis in young children are probably exceedingly common yet they have been relatively seldom described Various hypotheses have been advanced to explain these outbreaks, but their cause remains obscure We describe here two epidemics of acute bronchitis bronchiolitis, and bronchopneumonia in young children and examine possible infective causes in particular the influenza viruses

Rilliet and Barthez (1884) pointed out that the most severe forms of acute bronchitis in young children might occur in epidemics. Outbreaks of bronchiolitis have been described more recently in England by Hubble and Osborn (1941) in America by Adams et al (1942) Greengard et al (1941) Pratt (1944) Henderson and Rosenzweig (1951) and Walker (1952) and in France by Marquézy and Debray (1950) All described multiple cases of severe bronchitis, bronchiolitis or bronchopneumonia occurring within a relatively short time in children mostly aged less than 2 years.

The most likely of the possible causes seems to be one of the influenza viruses. For more than a century it has been known that in adults bronchitis and pneumonia are related to epidemic influenza (Ministry of Health 1920) and the increase in mortality associated with influenza is usually greatest in young children and old people (Burnet and Clark 1942) On the other hand West (1884) pointed out that catarrhal epidemics were not uncommon among the young when there was no general prevalence of the same class of ailments in the adult population. Again, Wollstein and Goldbloom (1919) mention that, when the pandemic of influenza started, there was a general impression that children were not affected by it. They themselves maintained however, that, as soon as the influenza spread from the Services to the civilian population the incidence of pneumonia in children did increase Hubble and Osborn (1941) noted that all their 50 cases of bronchiolitis occurred in the first ten weeks of 1940 although they suggested influenza as the cause they admitted that proved viral influenza was not prevalent in England at the same time. Anderson et al (1953) found that in Glasgow the greatest absolute increase in pneumonia notifications in the 1950–51 influenza A epidemic occurred in those aged 4 years or less On the other hand, during the same epidemic Semple (1951) in Liverpool Burn (1951) in Salford, and Fry (1953) in his practice in Kent noted that infants and young children seemed to be relatively unaffected Stuart Harris et al (1949) moreover pointed out that in Sheffield in December 1947 and January, 1948 when there was no epidemic of influenza, there were more notifications of and deaths from, pneumonia in children aged less than 5 years than in the corresponding months of the succeeding year when there was an influenza epidemic They also showed that the number of cases of pneumonia in children aged less than 5 years was greater in February, 1949 than in March 1949, at the height of the influenza A epidemic It therefore seems that the relationship between influenza and pneumonia in children aged less than 5 years is not so constant or precise as it is in adults.

Several workers have suggested that these epidemics might be due to the virus causing primary atypical pneumonia " associated with increased cold agglutinins in adults (Nelson and Smith 1945, Adams 1948, Thompson and Spector 1949, Walker 1952) Others have emphasised the importance of infections of the upper respiratory tract—e g , colds and " febrile catarrh "—in conjunction with bacteria in the pathogenesis of acute bronchitis in children (West 1884, Cruickshank 1939, Holt and McIntosh 1940, Moncrieff et al 1953)

Material and Methods

This study was restricted to the London area during the two winters of 1949–50 and 1950–51

CLINICAL AND EPIDEMIOLOGICAL STUDY

As an indication of the incidence of bronchitis and pneumonia in children aged less than 5 years, the admission dates of all cases so diagnosed at four London hospitals have been grouped together by weeks numbered in accordance with the Registrar-General's Weekly Returns All cases of acute bronchitis, bronchiolitis, and pneumonia have been included throughout both winters from week 40 to week 13 inclusive Children with primary tuberculosis, bronchial asthma, bronchiectasis, fibrocystic disease of the pancreas, and congenital heart disease with heart failure have been excluded so far as possible, as have been cases occurring after measles or after whooping cough The hospitals from which these figures were obtained were the Hammersmith Hospital (hospital A), in West London, the Hospital for Sick Children, Great Ormond Street (hospital B), in Central London, Whipps Cross Hospital (hospital C), in East London, and St Andrew's Hospital, Bow (hospital D), in East London The age incidence and sex-incidence have been recorded for the admissions to three of these (hospitals A–C) A broad clinical analysis has been attempted for the cases admitted to two (hospitals A and B), whereas the radiological, bacteriological, and serological findings are presented only for cases admitted to hospital A

The mortality from respiratory infections has been derived from the number of registered deaths from influenza, pneumonia, and bronchitis in London, abstracted from the Registrar-General's Weekly Returns

The extent and timing of the influenza B epidemic in the first winter and the influenza A epidemic in the second have been assessed by three criteria

(1) The percentage of patients of all ages with respiratory infections whose sera, examined at the Virus Reference Laboratory, Colindale, showed complement-fixing ant to influenza B and influenza A to a titre (reciprocal dilution) of 32 or higher The onset dates of these pat illnesses have been grouped together by fortnightly per

TABLE I—AGE AND SEX OF ALL CHILDREN WITH BRONCHIOLITIS, OR PNEUMONIA ADMITTED TO B, AND C

Age	1949–50		1950–51	
	Male	Female	Male	
Less than 6 mos	38	27	3[illegible]	
6–11 mos.	27	14	19	[illegible]
12–23 mos	18	10	23	[illegible]
Total less than 2 yr	83	51	77	
2 yr –2 yr 11 mos	15	8	11	[illegible]
3 yr –4 yr 11 mos	13	15	16	[illegible]
Total 2–4 yr (incl)	28	23	27	[illegible]

(2) The number of new claims to sickness benefit weekly, in the London and Middlesex region, to the of National Insurance (Massey 1951)

(3) The weekly number of registered deaths from pneumonia, and bronchitis combined for the age-group

BACTERIOLOGY AND VIROLOGY

In the first winter, throat swabs, taken as admission as possible, were plated on to blood In the second winter material was aspirated from nasopharynx with a soft rubber catheter through a sterile trap bottle to a mechanical apparatus, and plated on to chocolate agar (for *philus influenzæ*) as well as blood-agar Mouse i tion was also used for the isolation of pneum which were tested against sera of types I, II, vii, and viii

In both winters specimens of serum from children were examined by one of us (J W F) Hammersmith Hospital for cold agglutinins Spe were also examined at the Virus Reference Lab Colindale, for *Streptococcus M G* agglutinins complement fixing antibodies to the viruses of psitta influenza A, influenza B, and *Rickettsia burneti* (Q In the second winter hæmagglutination inhibition were also done on specimens of serum in the acute convalescent stages against influenza A (PR 8) influenza A prime (A/Ankara/1/51) strains

Attempts to isolate a virus were on material obtained from 5 cases first winter

Results

BRONCHITIS EPIDEMICS

During the two winters 497 ch aged less than 5 years were admitted bronchitis or pneumonia to the hospitals, there being 263 adm during the first winter and 234 durin second

In the first winter 216 cases (82%) admitted during the last three wee 1949 and the first seven weeks of and 166 of these within a six week p It can be seen from fig 1 that week 1 week 4 of 1950 show the highest fi with 38 and 37 admissions respecti During the whole winter there were registered deaths in children aged l 5 years in London from " influe pneumonia, and bronchitis, of which occurred during the ten-week epi period, the greatest number of being recorded in week 1 and of 1950

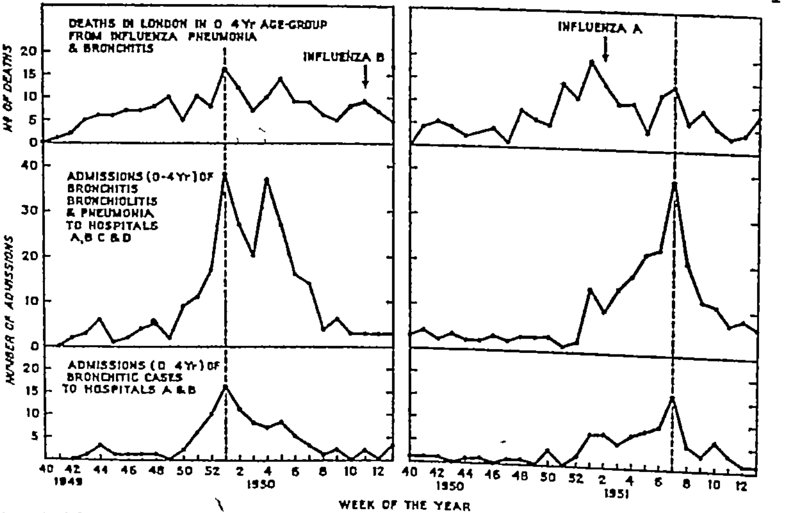

Fig 1—Timing of bronchitis epidemics Weekly number of admissions to four London hospitals of children aged less than 5 years with acute bronchitis, bronchiolitis, and pneumonia corresponds to an increase in the number of registered deaths in London pneumonia, and bronchitis. Peak of each influenza epidemic is indicated correspond to vertical interrupted lines in fig 2.

n the second winter there were 234 admissions, grouping of which also suggests an epidemic (fig 1) ough of the same duration it occurred three weeks r than in the previous winter There were 180 cases %) admitted in the first ten weeks of 1951 120 of n within a five-week period from week 4 to week 8 usive. There was only one peak of comparable in week 7 (with 38 admissions) although a lesser k (of 14 admissions) can be seen in the first week of New Year During the whole winter there were registered deaths in children aged less than 5 years ondon from 'influenza," pneumonia, and bronchitis, which 93 occurred in the ten week epidemic period t of the deaths took place in week 1 of 1951, and the t greatest number in week 7 (fig 1)

ical Analysis

f 364 children admitted to hospitals A, B, and C ly a third (117) were aged less than 6 months e than half (191) were aged less than 1 year and e than two thirds (252) less than 2 years Throughout winters there was a significant preponderance of e admissions which was chiefly restricted to children l less than 2 years (table I)

t hospitals A and B 217 cases were divided on the s of their physical signs into two groups; one with ralised signs of bronchitis (' bronchitic cases) the other with evidence of localised pulmonary lvement only (localised ' cases) It can be seen n table II that the bronchitic cases greatly out bered the localised especially during the height ch epidemic

he localised group (35 cases) was composed of a cellaneous collection of segmental or lobar pneu ins Except in the cases of staphylococcal pneumonia th empyema the children were not alarmingly ill ny time, and response to sulphonamides and/or biotics was rapid and clear cut. This group will be further considered here

he bronchitic group (182 cases) was made up of s of acute bronchitis, bronchiolitis, and broncho monia The chief clinical feature in most cases r dyspnœa of sudden onset usually following a few with a runny nose and cough Although there only 4 deaths (a mortality of 2 2%) many of these nts were alarmingly distressed, and 64 (30%) were ted in oxygen tents Nearly all the patients received either penicillin and sulphonamides, aureomycin or chloramphenicol. Recovery was usually rapid but not dramatic and the part treatment played in the outcome cannot be assessed in the absence of controls Some cases deteriorated after admission while on each type of treatment

E II—WEEK OF ADMISSION OF BRONCHITIC' AND LOCALISED CASES ADMITTED TO HOSPITALS A AND B IN TH WINTERS

k no	1949–50		1950–51	
	"Bronchitic" cases	"Localised" cases	Bronchitic cases	"Localised" cases
10			1	
11			1	
12			1	
13	1			
14	3		1	
15	1		1	
16	1			1
	1	1	1	
18	1	1	1	
19		1		1
20	2		3	
21	6	1		
	10		4	
1	16	1	7	5
2	11	2	7	
3	8	1	5	2
4	7	2	7	2
5	8	1	8	1
6	5	1	9	
	3	1	10	
8	1	1	6	1
9	2		3	1
10		1	6	1
11	2		3	2
12			1	3
13	3		1	
tal	92	15	90	20

TABLE III—SEROLOGICAL INVESTIGATIONS FOR INFLUENZA IN 13 CASES ADMITTED TO HOSPITAL A DURING BRONCHITIS EPIDEMIC OF 1951

Case no	Age		Week admitted in 1951	Day of disease	Complement fixation test (soluble) antigen)		Hæmagglutination inhibition tests		
	(yr.)	(mth.)			A	B	A(PR.8)	A/Ankara/1/51	B(Lee)
1		[illegible]	8	5 14	— 0	— 0	128 128	8 <8	<8 <8
2		1	7	5 02	— 0	— 0	64 32	<8 <8	16 <8
3		1¹/₄	7	7 16	0 0	0 0	32 32	<16 <16	<16 <16
4		9	7	9 18	— 0	— 0	128 128	<8 <8	8 8
5		4	10	10 43	— 0	— 0	64 64	<16 <8	32 32
6		6	10	4 14	— 0	— 0	<8 <8	8 16	<8 <8
		6	7	3 27	— 0	— 0	<8 <8	32 32	<8 <8
8		7	9	8 11	0 0	0 0	128 64	<8 <8	<8 <8
9	1		7	2 23	— 0	— 0	128 128	<8 <8	8 8
10	1	2	10	6 28	16 16	0 0	64 3	128 128	32 16
11	2	1	7	5 16	— 0	— 0	64 64	32 32	8 <8
12	2	3	6	5 60	— 0	— 0	32 32	<8 <8	8 <8
13	3	3	4	4 13	— 0	— 0	8 <8	<8 8	<8 <8

— = Not tested 0 = Titre less than 16

The X ray appearances of 65 bronchitic cases at hospital A were reviewed In 27 the films were normal 20 showed generalised patchy shadows or streaking interpreted as patchy collapse and emphysema and 18 showed definite evidence of consolidation

White-cell Counts

In 50 bronchitic cases from hospital A total and differential white-cell counts were normal in 38 in only 12 was the absolute polymorph-count more than 7500 and in only 8 more than 10 000

Bacteriology

In the first winter during the epidemic period of 29 throat swabs taken on admission from bronchitic cases 24 yielded only *Strep viridans Neisseria catarrhalis* or micrococci, 4 *Staphylococcus aureus* and only 1 *Strep pneumoniæ* of undetermined type

During the epidemic period of the second winter material was aspirated from the nasopharynx in 24 bronchitic cases: 16 yielded *Strep viridans N catarrhalis* or micrococci 7 *Strep pneumoniæ* (2 of type VIII 1 of type VII and 4 of undetermined type) and only 1 *H influenzæ*

Virus Studies

During the epidemic in the first winter specimens of serum from 14 convalescent bronchitic patients from hospital A were examined for cold agglutinins and the complement-fixing antibodies to psittacosis, influenza A

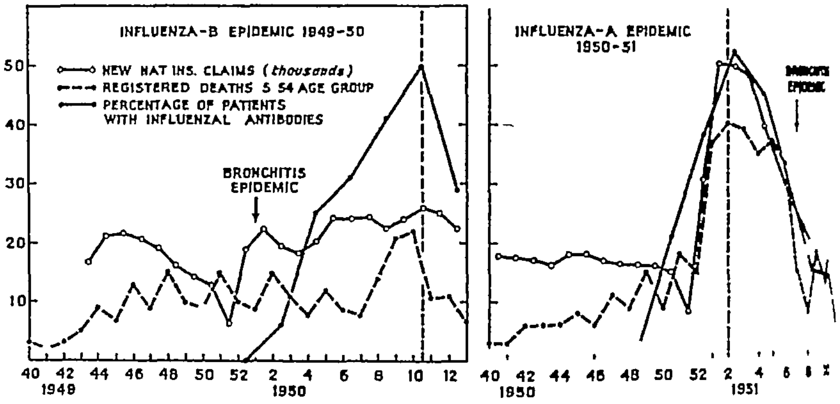

Fig 2—Timing of influenza epidemics judged by 3 criteria. Peak of each bronchitis epidemic by arrows which correspond to vertical interrupted lines in fig 1

influenza B, and Q fever All the tests gave negative results In addition necropsy material obtained from an infant, aged 8 weeks, who had died of bronchiolitis within twelve hours of the onset of his illness, was inoculated into fertile hens' eggs, ferrets, hamsters, and mice Throat washings from 3 other cases, obtained twenty-four hours, four days, and five days after onset respectively, were inoculated into fertile hens' eggs and hamsters No evidence of the presence of influenza or any other virus was obtained

During the epidemic in the second winter specimens of serum were similarly examined from 27 bronchitic cases, 25 were completely negative One boy (case 10 of table III), aged 14 months, showed an unchanging titre of 16 to influenza A on the 6th and 28th days of his illness A girl, aged 2 years, had a titre of 64 to influenza A on the 8th day of her illness and 32 on the 85th day These were the only cases in which complement-fixing antibody was detected, but titres such as these may persist for at least three months after infection with influenza Hæmagglutination inhibition (Salk) tests to influenza A (PR 8) and influenza-A prime (A/Ankara/1/51) viruses were done on paired sera from 13 of these children 10 showed a fixed or falling titre to influenza A (PR 8) (6 of these were infants aged less than 8 months and may have possessed passively acquired maternal antibodies, 4 were aged more than 1 year and therefore had probably acquired their antibodies as a result of previous infection), 3 showed a fixed titre to influenza A prime (A/Ankara/1/51), and 2 showed a low fixed titre to influenza B (Lee) In none of these cases did the findings, which are summarised in table III, suggest that any of the known influenza viruses had been responsible for any of the immediate illnesses

INFLUENZA EPIDEMICS

The influenza B epidemic in the first winter was mild in London It can be seen (fig 2) that, judged by the onset dates of the respiratory illnesses of patients examined for influenzal antibodies, it started soon after Jan 1, 1950, and reached its peak at week 10 or 11 The amount of clinical illness among the adult population associated with it was small, judged by the number of new claims to sickness benefit made each week to the Ministry of National Insurance, both the number of new claims and of registered deaths from "influenza," pneumonia, and bronchitis each week for the age-group 5–54 reached a maximum at about the same time

The influenza A epidemic in the second winter was by comparison severe There is good correlation between the percentage of cases showing influenza A antibodies, the number of new claims for sickness benefit, and the number of registered deaths from "influenza," pneumonia and bronchitis in the 5–54 age-group (fig 2)

Discussion

Epidemics of acute disease of the lower respiratory tract in children, aged less than 5 years, of sufficient severity to require admission to hospital occurred in London in each of the two winters of 1949–50 and 1950–51 Each lasted about ten weeks and was reflected in a simultaneous rise in the death-rate from respiratory disease in the same age group A clinical analysis of some of the cases admitted revealed that the epidemics were [illegible]iced by an explosive increase in the number of cases sharing in common the physical signs of a bronchitis About two thirds of this group had plicated acute bronchitis, and about a third bronchiolitis or bronchopneumonia We refer to together as the "bronchitic" cases and to the epi which they formed as the "bronchitis epidemics."

The occurrence of an epidemic of influenza B in 1950, and of influenza A in the winter of 19 provided an opportunity to study the relation these bronchitis epidemics to virus influenza. epidemiological observations suggest that virus was not in either winter the cause of the bro epidemics

(1) The bronchitis and influenza epidemics but did not coincide The peak of the bronchitis epi the first winter preceded the peak of the influenza B by ten weeks, that in the second winter followed the of the influenza A epidemic by five weeks

(2) The bronchitis epidemic during the winter of th influenza B epidemic (1949–50) was more severe than during the winter of the relatively severe influenza-A ep (1950–51)

Both these observations resemble those rep Stuart-Harris et al (1949) in Sheffield. The mor figures for the older age groups form a striking c being, as might be expected, much higher in the s winter, during the influenza A epidemic Al at the same time there was an increase in mo in children aged less than 5 years, this was smaller in the older age-groups, in contrast with the Anderson et al (1953) for Glasgow during the epidemic The weekly figures for London during winter (1950–51) show that there were two sep waves of deaths from disease of the respiratory in children aged less than 5 years, the first ass with influenza A and the second with the bro epidemic If both waves were grouped together single two month period, as done by Anderson (1953), the number of deaths attributed to infl in children aged less than 5 years would be undul These findings are against the view that influenza was the cause of the bronchitis epidemics

It is of interest that the first bronchitis epid coincided with that described by Marquézy and De (1950), who reported the puzzling finding of influe (hæmagglutination-inhibition) antibodies and cold tinins in many of the infants they studied C fixation tests on 14 of the children we exam however, showed no complement fixing antibod influenza virus A or B, no *Strep M G* or cold agglut and attempts to isolate a virus were also negativ 5 cases During the second bronchitis epidemic cases were examined by similar tests and 25 of were negative The 2 positive cases showed no ody titre and might have acquired their influenza ome time during the preceding influenza epidemic negative results in adults would exclude infection nfluenza virus However the reliability of the plement fixation and hæmagglutination inhibition in the diagnosis of influenza in children aged less 1 year is virtually unknown indeed there is an ation that their antibody response may be poor lter and Eliza Hall Institute 1951)

ie failure to isolate pathogenic bacteria from any a few cases in the present study and the normal rential white-cell counts in most of the cases suggest bacteria did not play an important part in the omics This conclusion is supported by the findings nderson (1953) and Landsman (1953), who could not late variations in the bacterial flora of the upper iratory tract, particularly pneumococci with the lence of infections of the lower respiratory tract in lren and suggested that an unknown factor possibly in nature" was the principal contributory agent ie production of pneumonia in infants

ie titres of cold agglutinins (up to 32) and of *Strep* agglutinins (up to 10) observed do not reach the s suggested as significant by Crofton et al (1951) used the same technique in adults These findings est that the bronchitis epidemics were not due to an atile form of primary atypical pneumonia with ased cold agglutinins moreover their explosive ure indicates a short incubation period whereas that primary atypical pneumonia is about two weeks dan 1949)

he bronchitis epidemics might possibly have been ed by one of the several viruses responsible for the mmon cold and febrile catarrh which commonly t adults throughout the winter Neither the mortality res for the younger adult age groups, however nor figures for new claims to the Ministry of National rance suggest the presence of a simultaneous emic among the general population

i conclusion epidemics of a bronchitic illness broke among young children in London during the winters 949–50 and 1950–51 both were epidemiologically inct from influenza No evidence was obtained they were caused by a specific bacterium influenza s A or B psittacosis virus *R burneti* or the virus primary atypical pneumonia Their ætiology ains unknown

Summary

tudy of 407 children aged less than 5 years, with nchitis bronchiolitis and pneumonia admitted to London hospitals in the winters of 1949–50 and 0–51 showed that there was an epidemic of bronchitic ss lasting about ten weeks in each winter

he occurrence of these epidemics coincided with an ease in the number of registered deaths from fluenza, pneumonia, and bronchitis in children aged than 5 years in the London area

he bronchitis epidemic in the first winter was the re severe it preceded a mild influenza B epidemic bronchitis epidemic in the second winter was milder followed a relatively severe influenza A epidemic

Only 2 of 41 children examined serologically possessed ibodies to influenza virus and neither showed a rise of e No case showed a significant titre of Q fever or psittacosis antibodies, or of *Strep M G* or cold lutinins nor did cultures from the nasopharynx gest a bacterial cause

he ætiology of these outbreaks remains obscure

o wish to thank Dr Hilda Boffa Dr D R Barry Dr M lard and Dr O G Jones, of the department of bacteri y of the Postgraduate Medical School of London for bacteriological investigations; Dr B P Marmion he Virus Reference Laboratory Colindale for the attempts isolate a virus and the serological studies Dr C E. Newman Dr D MacCarthy Dr T P Mann and Dr A. P Norman for permission to investigate their cases Dr E Hindon Dr B D R Wilson and the medical committee of the Hospital for Sick Children, Great Ormond Street for allowing access to their case notes and records and Dr W P D Logan Dr E Hinden, and Dr B P Marmion for help and advice in the preparation of this paper

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SUDDEN OR UNEXPECTED NATURAL DEATH DUE TO RUPTURED INTRACRANIAL ANEURYSM

SURVEY OF 250 FORENSIC CASES

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Sudden or rapid death due to ruptured intracranial aneurysm is not uncommon According to forensic pathologists (Simpson 1947 Helpern and Rabson 1950) it accounts for 4–5% of all sudden and unexpected natural deaths At first sight this seems to be a completely unprofitable therapeutic field, but a few of these patients exhibit features either before or at the time of the fatal rupture which if they could be recognised in time might lead to surgical intervention and to prevention of the fatal outcome

Our study is based on 250 consecutive deaths due to ruptured intracranial aneurysm which were examined post mortem by Dr Keith Simpson Most of these cases were examined at the request of the coroner because the patient either had been found dead or had died quickly and unexpectedly Two fifths of the patients had survived long enough to reach hospital but more than half of these had died shortly after admission In the remaining cases, about a sixth of the total death had been delayed for a day or more but no satisfactory diagnosis had been made Dr Simpson kindly made available to us in his records not only his necropsy findings but also the salient features of the

TABLE I—AGE AND SEX IN 250 CASES OF RUPTURED ANEURYSM CAUSING SUDDEN DEATH

Age (yr)	0–9	10–19	20–29	30–39	40–49	50–59	60–69	70–79	
Males	0	3	1	14	16	21	21	9	
Females	0	1	4	7	18	36	50	36	
Total	0	4 (*1 6%*)	8 (*3 2%*)	21 (*8 4%*)	34 (*13 6%*)	57 (*22 8%*)	71 (*28 4%*)	45 (*18 0%*)	10 (4

clinical history Consequently we have been able to analyse these records to determine whether there are any significant differences between forensic cases and those ordinarily seen in hospital practice, and what proportion of the deaths might have been forestalled by prompt diagnosis and surgical treatment

Clinical Features

Age distribution—Just over half the deaths were of people aged 50–70 (table I) This is in keeping with most recently published reports of large series of intracranial aneurysms from hospital practice (Richardson and Hyland 1941, Hamby 1948, Hyland 1950, Ask-Upmark and Ingvar 1950) Leaking aneurysms do not, as is sometimes stated, occur chiefly in young persons They can occur at any age, and in each decade the prognosis is serious, the over-all mortality rate observed in most general hospitals being more than 50% (Falconer 1951), but there is no doubt that the prognosis worsens with advancing age, pari passu with the progress of widespread degenerative vascular disease

Sex distribution—Of the 250 patients 159 were female and 91 male, a ratio of 5 to 3 A similar slight preponderance of females was noted by Ask-Upmark and Ingvar (1950) and Meadows (1951) and is apparent in statistics relating to deaths in this country (Registrar-General, personal communication) However, in Dr Simpson's patients aged more than 50, females outnumbered males by 2 5 to 1, with aneurysms of the posterior cerebral artery the ratio was 3 to 1, and with aneurysms of the basilar and vertebral arteries 4 to 1 The reason for this curious preponderance of females is not known, but the preponderance is found in both forensic and hospital cases

Antecedent Stress or Trauma—In most of the forensic cases there was sufficient information to show whether an episode of undue physical exertion had either coincided with or shortly preceded the rupture, such an occurrence was noted in only 10 cases (4%) This again is in keeping with the observation of Magee (1943), that, in Service personnel who develop subarachnoid hæmorrhage, trauma or stress occurred as an apparent precipitating factor in only 8% It is perhaps noteworthy that no head injury was found in any of the forensic cases

Premonitory Symptoms—In this forensic series many patients had complained for some weeks or even months of slight or moderate headaches or of attacks of dizziness, but, in view of the frequency with which such non-specific symptoms occur in the general populace, in few patients could such symptoms, even in retrospect, have been identified at the time as premonitory Indeed in 164 cases (66%) the fatal attack seemed to come like a bolt from the blue It is noteworthy, however, that in 23 cases (9%) there was a previous history of subarachnoid hæmorrhage occurring from sixteen days to ten years earlier Such an incidence of previous attacks of hæmorrhage is also often apparent in hospital case-material

Necropsy Findings

Distribution of Aneurysms—274 aneurysms were found in the 250 cases, multiple aneurysms being noted in 6% of cases, a figure which is not out of the ordinary The various aneurysms were equally distributed between the right and left sides Their distribution seems comparable with that in unoperated hospital cases studied post mortem and with that in cases surgically (table II), except that at first sight it that in Dr Simpson's material there was a aneurysms situated on the supraclinoid portion internal carotid artery and an excess of the middle cerebral artery A possible explanation that it is often very difficult at necropsy, when the cisterns are solid with clot and the arterial is distorted, to decide just where the internal artery ends and the middle cerebral artery Arterial injection, by giving pictures of the arrangement comparable to those afforded in the by carotid arteriography, might prove very here Perhaps, therefore, some of the labelled as being on the middle cerebral artery actually situated on the internal carotid artery so, there may be no significant differences between distribution of aneurysms in forensic cases and in hospital cases This point will require further study

Other Findings—The size of an aneurysm to have no direct bearing on the severity of the rhage to be expected from it This forensic included aneurysms of all sizes from 1–2 mm in up to large aneurysms 4 cm in diameter, but in con with hospital experience most of the aneurysms small Intracerebral bleeding as well as subarac bleeding was often found with aneurysms of the an cerebral and anterior communicating arteries and of middle cerebral artery, a finding which agrees with in hospital material (Richardson and Hyland Robertson 1949) Dr Simpson also noted that only 80 cases (32%) was there a degree of atheroma cerebral vessels which was worthy of comment Fr in the patients aged more than 40 the incide cardiovascular disease, judged by definite hyper cardiac changes and/or noteworthy atheroma was 64% The importance of these conditions in predisp to rupture is therefore difficult to assess, for they are primary factors, and a similar incidence of cardi disease might well be expected in illness other aneurysm in comparable age groups (Meadows 1951)

TABLE II—COMPARISON OF DISTRIBUTION AND LOCA RUPTURED ANEURYSMS IN ORDINARY HOSPITAL AND FORENSIC CASES

Arteries	Fatal unoperated hospital series—37 aneurysms (Richardson and Hyland 1941)		Operated hospital series—70 aneurysms (Falconer 1952)		[illegible]
Internal carotid	26%	56%	47%	64%	2%
Middle cerebral	30%		17%		46%
Anterior cerebral	33%		32%		33%
Vertebral basilar, and posterior cerebral	11%		4%		[illegible]

Discussion and Conclusions

There thus appears to be no striking difference be this series of forensic cases and the ordinary ru hospital cases as regards age and sex, location aneurysms, and such predisposing factors as size of aneurysm, and pre existing cardiovascular e only striking difference so far apparent concerns the ration of symptoms for whereas in the hospital aterial the clinical course is usually sufficiently pro nged not only to enable the patient to reach hospital t also to permit of a correct diagnosis, in the forensic ses death was generally sudden rapid or unexpected ven when the forensic cases did reach hospital death ually took place so soon afterwards that it seems first sight that little could have been done to forestall

Indeed there may be little time even for diagnosis us in the whole series an approximate antemortem agnosis was forthcoming in only 57 cases (20%) d the correct diagnosis of subarachnoid hæmorrhage as made in only 17 cases (7%)

The question arises whether any of these deaths could ve been prevented either by prophylactic investigation d treatment before the fatal rupture or by prompter agnosis after rupture had occurred Until recently ch a consideration would have been academic and practical for the routine treatment of bleeding eurysms has been merely a matter of rest and quiet d in these circumstances earlier diagnosis in the forensic ses would have made little difference to the outcome t surgery is now making strides in this field and ports are appearing from several surgical centres owing that after the aneurysm has been first located d demonstrated by cerebral arteriography prompt rgical intervention can reduce the expected mortality more than 50% to a third or even less (Falconer 51, 1952 Mount 1951 Norlén 1952) Further experi ce may even improve these results and we have ely had a consecutive series of 20 recently bleeding eurysms operated on by either arterial ligation or aniotomy without a death The prospects for surgery non bleeding aneurysms should be even better because fferson (1952) and Johnson (1952) treated 113 such ses by carotid ligation without fatality

In this connection two important points emerge rstly in 23 (9%) of Dr Simpson s cases there was previous history of subarachnoid hæmorrhage from teen days to ten years earlier Subsequently when e fatal recurrence came, 18 of these patients died thin twenty four hours and only 5 survived for longer riods up to a week There would be thus little or opportunity to treat such patients if one had to wait til the second and probably fatal rupture Recurrence bleeding is an ever present risk with intracranial eurysms and although most recurrences occur while e patient is still in hospital under treatment for his st attack (Magee 1943, Falconer 1951) even after scharge from hospital there is a 20% chance of fatal current bleeding if patients are followed up for six ars or more (Hyland 1950) Considering that per taneous cerebral arteriography is fairly safe we feel at all patients who have had even a single and mild tack of subarachnoid hæmorrhage should be investi ted in this way and that, if an aneurysm is found me operation to lessen or prevent rupture should en be carried out To postpone cerebral arterio aphy until recurrent bleeding has appeared leads to e surgeon s being called on to treat the underlying dion under unfavourable conditions, and all too often the patient s death before appropriate treatment can en be started

The second point is that in 38 cases (15%) death s delayed for more than twenty four hours after the pture and in 15 of these for more than a week All t 3 of these patients had been in hospital sufficiently ng to be operated on if the correct diagnosis had en made and the necessary ready access to a neuro rgical centre had been available None however was treated.

Thus 56 cases in this forensic series (22%) exhibited ne feature which had its significance been recognised should have paved the way for precise diagnosis and treatment Not all of these patients of course would have survived, even in the best surgeon's hands but possibly a proportion could have been salvaged at least more than a half. The evidence therefore indicates that even in such a highly unfavourable selection of bleeding aneurysms as the forensic series just considered some of the deaths could have been prevented

We wish to thank Dr Keith Simpson for his kindness and encouragement

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ALKALOSIS IN INFANTS

TREATMENT BY INTRAVENOUS INFUSION OF AMMONIUM CHLORIDE

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Severe alkalosis can be rapidly relieved by infusing ammonium chloride intravenously but the fear of toxic reactions and the need for biochemical control have prevented this from becoming a common therapeutic measure

Adults with alkalosis have been treated successfully with intravenous ammonium chloride (McCann 1922 Youmans and Greene 1925 Zintel et al 1943 Grace and Barr 1948) Forbes and Erganian (1946) gave nine infants with pyloric stenosis and alkalosis a solution of M/6 ammonium chloride in either isotonic saline solution or Ringer's solution by subcutaneous or intravenous routes for the relief of their alkalosis. These workers could not collect enough urine to report significant findings

Since more data are required on the effectiveness and safety of intravenous ammonium chloride in infants before this treatment can be advocated for them we report here the changes in clinical condition blood chemistry and urine findings resulting from the infusion of ammonium chloride in seven infants.

Material

Five (cases 1-5) of the seven babies had pyloric stenosis and alkalosis and were aged 2-11 weeks The two other infants (cases 6 and 7) who both had hydrocephalus and were aged 4 months, were in a good state of nutrition and hydration and showed no abnormality in acid base balance

Methods

Procedure

The babies with pyloric stenosis were seen soon after admission while dehydrated and alkalotic Specimens of

EFFECT OF INTRAVENOUS AMMONIUM CHLORIDE ON PLASMA-CARBON DIOXIDE AND PLASMA CHLORIDE LE SEVEN INFANTS

Case no	Age (weeks)	Weight (g)	Infusions before ammonium chloride	Infusion of ammonium chloride 0 89 g per 100 ml			Time between ammonium chloride and next blood collection (min)	Plasma carbon dioxide before ammonium chloride (m eq per litre)	Fall in plasma carbon dioxide level		Plasma chloride level before amm. chlor (m.eq per litre)
				Volume infused (ml)	Infusion time (min)	Amount infused (ml per kg of body weight)			(m eq per litre)	(m eq per litre per ml amm chlor per kg of body weight)	
1	11	3500	Glucose 80 ml	150	120	43	9	40	16	0 37	105
2	2	3270	$^1/_5$ isotonic saline solution in glucose 200 ml	150	270	46	300	41	16	0 35	76
3	4	3300	$^1/_5$ isotonic saline solution in glucose 150 ml	100	135	30	300	33 5	14 5	0 48	8
4	6	4100	$^1/_5$ isotonic saline solution in glucose 100 ml	250	285	61	60	39	15	0 25	63
5	7	4200	$^1/_2$ isotonic saline solution in glucose 200 ml	80	90	19	35	32	0	0 0	75
6	16	3850	$^1/_5$ isotonic saline solution in glucose 50 ml	90	74	15	23	22	13 5	0 9	109
7	16	7970	Glucose 145 ml	80	72	10	8	21	2	0 2	99
										Average = 0 43	

blood for analysis were taken from either the femoral vein or the sagittal sinus, and fluids were given via the scalp veins The first infusion was either 5% (*w/v*) glucose, or $^1/_5$ isotonic saline solution (0 18 g per 100 ml) in 4 3% (*w/v*) glucose, or $^1/_2$ isotonic saline solution in 4 3% (*w/v*) glucose The second infusion was aqueous *M*/6 ammonium chloride (8 9 g ammonium chloride per litre of water) The fluids were given slowly at rates varying from 0 5 to 1 5 ml. a minute The dose of ammonium chloride depended on the initial plasma carbon dioxide level and the reduction desired, on the assumption that 1 ml of *M*/6 ammonium chloride per kg of body-weight would reduce the plasma carbon-dioxide level by 1 vol per 100 ml During the infusions nothing was given to the infants by mouth Urine was collected through a many-holed catheter into a receptacle containing toluene and liquid paraffin

Analytical Methods

Heparinised plasma from blood collected under liquid paraffin was used for the determination of the carbon-dioxide level in either the manometric or volumetric apparatus of Van Slyke (1917) and Van Slyke and Neill (1924) The plasma chloride level was determined by Sendroy's (1937) method on 0 2 ml of plasma Sodium was precipitated as sodium zinc uranyl acetate and estimated by the modification of Butterworth (1951) The pH of the urine was determined as quickly as possible with a glass electrode and a Marconi pH meter Titratable acidity was estimated by titrating the urine against *N*/10 sodium hydroxide to pH 7 4 with phenol-red as indicator and a Lovibond comparator The method advocated by King (1951) was used for estimating ammonia These latter two methods were only sensitive enough to show large differences in the excretion of ammonia and titrable acidity

Results

Clinical

The clinical condition of the five babies with pyloric stenosis and alkalosis improved during the preoperative period They were quiet, and hunger and vomiting was not a problem The two infants with hydrocephalus remained well throughout their infusions

Blood Chemistry

The response to the infusion of aqueous *M*/6 ammonium chloride is shown in the accompanying table Four babies with pyloric stenosis (cases 1–4), who received 30–61 ml of ammonium chloride per kg of bod showed a fall in plasma carbon dioxide level of 14–1 per litre This was balanced by a rise in the p chloride level of 11–16 m eq per litre in the three (cases 1, 2, and 4) in whom it was estimated babies had received either glucose or $^1/_5$ isotonic solution in glucose immediately before the amm chloride The fifth infant (case 5) was given $^1/_2$ saline solution in glucose followed by 19 ml of chloride per kg of body-weight Technical diffic prevented the infusion of more ammonium chl and the amounts given did not reduce the plasma- dioxide level, although the plasma chloride level slightly (4 m eq per litre)

The two babies with hydrocephalus were g ammonium chloride at the rate of 10–15 ml per k body weight A response was observed in case 6, w plasma-carbon-dioxide level had fallen by 13 5 m eq litre twenty-three minutes after the end of the inf This fall was offset by a rise in the plasma-chloride of 8 m eq per litre

There was a significant change in the serum-so level in one of the three infants in whom this determi- tion was done the serum sodium level of case 4 was m eq per litre immediately before the infusion ammonium chloride, but six hours later, an hour a the infusion had ceased, it had fallen to 122 m eq litre Nine hours later the serum-sodium level was m eq per litre Parallel changes in the sum of chloride and carbon-dioxide levels were observed

Renal Response

The infusion of ammonium chloride was al preceded by either $^1/_5$ isotonic saline solution in gluc 5% (*w/v*) glucose It was therefore difficult to att any changes in minute volume and pH of the urine changes in the excretion of ammonia and titra acidity, to ammonium chloride alone There was, h ever, a pronounced difference in the diuretic respon the three dehydrated infants with pyloric ste (cases 1, 3, and 4) and the two normally hydrated inf (cases 6 and 7) The volume of urine excreted by dehydrated infants was not appreciably changed infusing ammonium chloride, and the urine mi volume was much lower than the rate of infusion, wh the two babies with hydrocephalus excreted such la volumes of urine that the minute volume approached exceeded the rate at which the infusion was given

-The pH of the urine remained 6 8–7 0 in two of the ro infants with pyloric stenosis (cases 1 and 3) and in se 4 *with pyloric stenosis there were falls in urine pH* m 7·0 to 5 8 and to 6 4 The pH of the urine in the o normally hydrated infants was 5·8–6 7 showing a idency to fall after the ammonium-chloride infusion t a high urine minute volume at that time masked y significant effect

The excretion of ammonia and titratable acidity during d after the infusion of ammonium chloride was studied four cases The amount of ammonia and titratable idity excreted in unit time was low and almost constant cases 1 and 3 with pyloric stenosis, in whom the pH is uniform. The two well hydrated infants (cases 6 d 7) excreted more ammonia in unit time when the ine minute volume rose The excretion of titratable idity in unit time was very low during the periods of idy

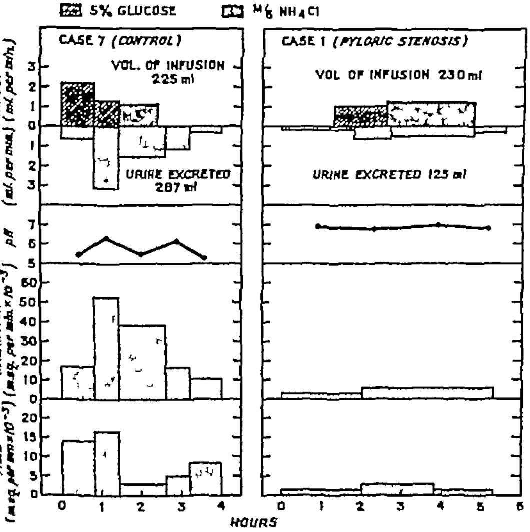
The results obtained in cases 1 and 7 are contrasted the accompanying figure

Toxicity

Cases 3 and 4 with pyloric stenosis developed genera ed convulsions In case 3 the convulsions occurred ien the baby had received intravenously 450 ml. of id containing 0 63 g of sodium chloride and had ssed only 30 ml of urine In case 4 the convulsions curred two and three quarter hours after the end of e ammonium-chloride infusion, when the infant had ceived 420 ml *of fluid containing* 0 3 g of sodium loride The serum-sodium level in case 4 fell from 0 m eq per litre just before the ammonium-chloride fusion to 122 m eq per litre six hours later

Discussion

The clinical condition of the infants with pyloric enosis improved before operation and hunger and stlessness were not appreciable Clearly it is impossible say whether these improvements were due to the ammonium chloride alone or to the intravenous fluids in general



rinary response of a dehydrated infant with pyloric stenosis (case 1) and of an infant in a good state of health and nutrition (case 7)

The fall in plasma-carbon-dioxide level to be expected from the infusion presents some problems (Bodansky 1949) Assuming that two thirds of the body weight was body water, and that the ammonium chloride given either intravenously or subcutaneously would permeate through the body water Forbes and Erganian (1946) calculated that the administration of 1 ml of *M/6* ammonium chloride per kg of body weight would reduce the plasma-carbon-dioxide level by 0 56 vol per 100 ml or *0 25 m eq per litre The decrease* which they observed was greater than this, and they *suggested that the* calculations ought perhaps to be based upon extracellular fluid and not on total body water Figures for the percentage of body weight occupied by the extracellular fluid of an infant obtained by the most reliable method (inulin) are not available Gamble s (1951) assumption that the extracellular fluid of an infant constitutes 25% of the body weight is compatible with the higher values *for sodium and thiocyanate space obtained* by Fellers et al (1949) in young infants, and for Na^{24} space in newborn infants (Flexner et al 1947, Perley et al 1951)

On the assumption that 25% of the body weight is a reasonable figure for the extracellular fluid of an infant aged 2–16 weeks the fall in plasma-carbon-dioxide level expected when 1 ml. of *M/6* ammonium chloride is infused is 0 67 m eq per litre This is considerably higher than the average falls observed However evidence has been *accumulating that about a third of the total body* chloride is intracellular (Deane et al 1952 Steele 1950) and it seems possible that the chloride infused would be distributed in the proportion of two thirds to the extracellular compartment and a third to the intracellular compartment In this event two thirds of the infused chloride would be available for reducing the plasma bicarbonate *level In these circumstances a fall of* 0 45 m eq per litre or 1 vol per 100 ml in the plasma carbon-dioxide level would be *expected from the adminis*tration of 1 ml of *M/6* ammonium chloride per kg of body weight. This figure is close to our *own* results and to the average result of Forbes and *Erganian (1946) which was 0 39 (range* 0 15–0·8) The average fall in our seven cases was 0 43 (range 0 00–0 9) whereas for the four cases of pyloric stenosis in which the calculated amount of ammonium chloride was given the fall in plasma carbon-dioxide level was *0 36 m eq per litre of plasma per ml* of *M/6* ammonium chloride per kg of *body weight (range 0 25–0·48) Thus* the fall in the plasma-carbon dioxide level after the infusion of ammonium chloride suggests that only two thirds of the infused chloride is available for *the reduction of the plasma bicarbonate* level in the extracellular fluid

The urine changes found by us could not be attributed to ammonium chloride alone, because of preceding infusion of saline solution or of glucose saline solution and these changes are not *therefore directly comparable with the* changes observed after the oral admini*stration of ammonium chloride in adults* (Sartorius et al 1949) and infants (Gordon et al. 1948) However there was a pronounced difference in the diuretic response between the normal *infants and those with pyloric stenosis* The latter were presumably deh ed and also in a state of sodi tion, and the lack of sodium for excretion may have been responsible for this difference The fall in pH which is expected after ammonium chloride infusion was masked by diuresis in the two children with hydrocephalus (cases 6 and 7) The increase in the amount of ammonia excreted during the periods of diuresis in these two children supports Wolf's (1947) contention that the excretion of ammonia is primarily a function of urine pH and does not suggest that any appreciable amount of the infused ammonium chloride was passing into the urine

The convulsion which occurred in two of our babies with pyloric stenosis treated with infusions of ammonium chloride were different from the toxic reactions reported previously Zintel et al (1943) described one febrile reaction and two complaints of scotoma during infusions of ammonium chloride to twelve adults Karr and Hendricks (1949) reported very severe reactions in dogs when ammonium salts were infused at a rate greater than 1 m eq per kg of body-weight a minute During preliminary experiments on dogs and rabbits Forbes and Erganian (1946) induced excessive salivation, hyperpnœa, and drowsiness when 20–30 ml of *M*/6 ammonium chloride per kg of body weight was infused intravenously in forty five minutes, and stupor and convulsions resulted when the speed of the injection was increased. They observed one toxic reaction in their nine infants with pyloric stenosis when 30 ml of *M*/6 ammonium chloride per kg of body-weight was infused in eighteen minutes This infant developed transient pallor, irregular respiration, brachycardia, and occasional twitching of the eyelids and hand Forbes and Erganian (1946) and Karr and Hendricks (1949) concluded that the toxicity of the infused ammonium chloride was directly related to the speed of the infusion It is unlikely that the convulsions observed in the present investigation were caused by the toxicity of ammonium ions, because the rate of infusion was less than 0 04 m eq per kg of body-weight a minute, and because of the nature of the reactions and the delayed onset after the infusion ceased Evidence that these convulsions were due to " water intoxication " is examined in a separate article to be published by two of us (S A D and K S H)

Mild cases of alkalosis can be satisfactorily treated with intravenous saline solution, but severe cases may need a more rapid relief of the alkalosis because of the risks of tetany and irreversible renal damage Some workers have treated severe alkalosis with ammonium chloride in either isotonic saline solution or in Ringer's solution Such a procedure makes it difficult to treat the patient as an individual and to calculate the fall in plasma-carbon dioxide level which a given dose of ammonium chloride should produce , yet it is undoubtedly necessary to replace the sodium and other electrolytes which have been lost by vomiting (Gamble and Ross 1925, Gamble and McIver 1925) Our findings suggest that the sodium lost should be replaced and dehydration relieved, preferably with $^1/_2$ isotonic saline solution, before attempts are made to correct the alkalosis The present investigation shows that the intravenous infusion of ammonium chloride for the relief of alkalosis in infants is safe if given slowly to a child who is not in a state of sodium depletion

Summary

Aqueous *M*/6 ammonium chloride was given intravenously to seven infants five with pyloric stenosis and alkalosis, and two with hydrocephalus who showed no abnormality in acid base balance

On the assumption that two thirds of the infused chloride is available to lower the plasma carbon dioxide level of the extracellular fluid, the fall expected from the infusion of 1 ml of *M*/6 chloride per kg of body-weight is 0 45 m eq per litre The fall observed by us was 0 43 ([illegible] m eq per litre) The infusion of glucose and glucose saline solution before the infu ammonium chloride prevented the study of the response to ammonium chloride alone, but the in the two controls was significantly greater tha infants with pyloric stenosis and alkalosis

Generalised convulsions developed in two cas pyloric stenosis, but these were not caused by ammonium chloride They were thought to be of " water intoxication "

The intravenous infusion of ammonium chloride effective and rapid method of correcting alkalos is safe when adequate precautions are taken

We wish to thank Prof R S Illingworth for his adv the preparation of this paper , Miss E Finch, M SC, for cooperation , Dr J L Emery for laboratory faci advice , and the nurses of the Children's Hospital, for their help The solutions of ammonium chlorid intravenous use were supplied by Allen & Hanburys Ltd

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HEXAMETHONIUM IN POLYVINYLPYRROLIDONE

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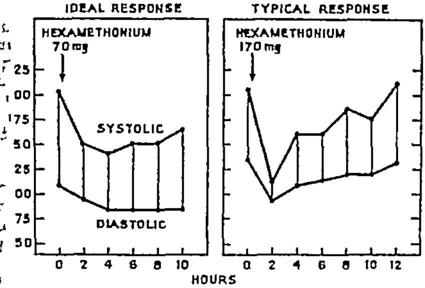
MORE than three years' study of the therapeutic of the methonium compounds in hypertension provided abundant evidence of their value (C and Robertson 1950, Smirk and Alstad 1951, Mackey Shaw 1951, Murphy 1951) Since the aim of to produce a sustained lowering of the blood pressure duration of effective action by the different routes great importance This is summarised in the accompanying table The duration of effect by the subcuta route has been shown to increase with the size of the d Most workers prefer this route, for action is pre and the patient can give himself the injections

DURATION OF EFFECT

Route	Action starts in	Maximal effect in (min.)	Duratio actio (hr.)
Oral	Up to 7 hours	—	6
Subcutaneous	15–30 minutes	25–30	3
Intramuscular	—	30	5
Intravenous	About 2 minutes	5	1-2

(See Mackey and Shaw 1951 Smirk and Alstad 1951 1951 Masini and Rossi 1951 Finnerty and Freis 1950, Kil and Smirk 1952)



1—Ideal and typical responses of blood-pressure to hexamethonium

o maintain the blood pressure within the desired its throughout the active part of the day it is necessary give three injections (Freis 1951) To obviate the need this various methods have been used

1) Combined oral and parenteral therapy with or without r drugs (Freis 1951)

2) The addition of vasoconstrictors to the injection irk and Alstad 1951)

3) Solution in a medium which delays absorption (almond dextran or polyvinylpyrrolidone [Smirk and Alstad 1951 ini and Rossi 1951])

4) Continuous injection throughout the twenty four hours an electrically operated syringe (Smirk 1951)

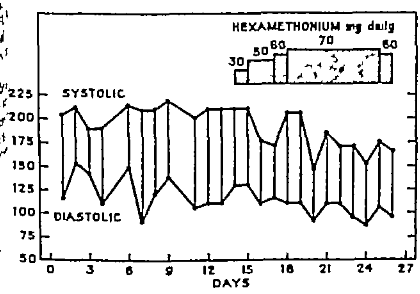
Most of these methods are ineffectual or impracticable solutions in polyvinylpyrrolidone are worthy of ther trial The solvent is a plasma substitute and was first used to delay the absorption of the solute Masini and Rossi (1951) later Smirk (1952a and b) orted on it favourably There is no evidence that solvent is harmful in the dose used or that it agonises the effect of hexamethonium

Investigation

We have therefore investigated the duration of effect blood pressure of one subcutaneous injection a day a solution of 20% hexamethonium bromide (*w/v*) in lyvinylpyrrolidone with 0 5% chlorbutol added as a servative and tried to find whether the size of the se modifies the effect No attempt has been made to dy the cases over a long period.

Five cases with severe hypertension, severe symptoms, d a grade III or grade IV retinopathy (Wagener and ith 1930) were studied All were submitted to a ndard routine of investigation designed to eliminate primary causes of hypertension cases with any evidence of coronary or cerebral arterial disease were excluded All had electrocardiographic changes indicating hypertension and enlarged left ventricle on radiography All were proved to be sensitive to an aqueous solution of intravenous hexamethonium One had been treated with dehydrogenated alkaloids of ergot (Rothlin 1952) with little success The patients were kept in hospital for fourteen days before treatment was started they were ambulant but not allowed unusual exercise Their blood pressures during this period were recorded daily with the patient standing at the same time and so far as possible, by the same person All satisfied the definition of hypertension given by Evans (1949)—i e a blood pressure of 190 mm Hg systolic and/or at least 110 mm Hg diastolic on three successive occasions in the presence of clinical radiological, and electrocardiographic evidence of arterial change

The initial dose determined by a modification of the Freis test (Murphy 1951) was given subcutaneously Great care was taken that the dose was accurately measured and that the needle was not accidentally inserted into a vein Blood pressure readings were then taken, under the conditions specified above at two hour intervals until the tenth or twelth hour



2—Cumulative effect of hexamethonium on blood-pressure ecorded on each occasion before the daily dose of this substance.

Results

An ideal response and a typical response of the blood pressure are shown in fig 1

In most cases the minimal systolic and diastolic blood pressures were reached within the first four hours but in one case it was reached at the eighth hour Appreciable hypotensive effect was at times apparent for as long as twelve hours. Considerable variation was noted from day to day with constant dosage despite careful measurement of the preparation by the doctor or by a senior nurse because the solution is viscous and more difficult to handle than the aqueous solution.

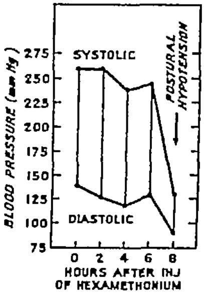


Fig 3—Late onset of postural hypotension after hexamethonium

The duration of action of the preparation does not seem to depend on the dose but to prove this it would be necessary to space the doses at intervals of days to obviate the effect of the development of tolerance

Evidence of cumulative effect was noticed in one case (fig 2) Although there was some variation there was a downward trend in the blood pressures even where the dose was kept constant

The side-effects noted were dizziness postural hypotension, constipation, loss of appetite and intestinal distension and colic There appears to be no lessening of the intestinal and other side-effects of hexamethonium, though the incidence of postural hypotension is lower Usually faintness and postural hypotension were noted in the first two hours In several cases however they came on late (fig 3) Though this may be due to the masking of hypotension in the earlier readings by physical activity the possibility that it is due to irregular absorption from the depot must also be borne in mind This unpredictability of the development of hypotension is more inconvenient than that from simple aqueous solutions of hexamethonium and in one case was gravely incapacitating

Summary

Hexamethonium in polyvinylpyrrolidone seems to have an effective hypotensive action which persists for six

to twelve hours and in some cases throughout the twenty-four hours, with a slight tendency to be cumulative Provided that its effect is constant throughout twelve hours (and this cannot always be achieved), one injection of the preparation given in the morning will suffice, because blood-pressure naturally falls at night Irregularities of action, with the production of postural hypotension, however, lessen its value

Our thanks are due to Dr L Glick and Dr J H Follows for permission to publish results on some of their cases, and to the former for his advice, and to the sisters and nurses of the Halifax General Hospital for their patient industry in taking hundreds of blood pressure readings Messrs May & Baker supplied the hexamethonium bromide in polyvinyl pyrrolidone and much otherwise inaccessible information

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A NEW METHOD FOR THE DIFFERENTIATION OF SICKLE-CELL ANÆMIA FROM THE SICKLE-CELL TRAIT

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Two recent discoveries of fundamental importance have given new interest to the study of the sickle cell anomaly

The first is the recognition of the fact that sickle cell anæmia (S C A) is far from rare on the African continent Before 1950 only sporadic cases of this condition had been reported there, although it was well known that 25% of natives of Central Africa harbour the asymptomatic sickle cell trait (S C T) Until very recently Raper's (1950) estimate that only one African in more than a thousand carriers of the trait develops S C A had never been contested seriously, but in 1951 Lambotte Legrand and Lambotte-Legrand, working at the Red Cross children's hospital at Leopoldville, reviewed 100 cases of S C A in African children, and Foy et al (1951), in Kenya, confirmed the high incidence of S C A in babies under twelve months of age

The second discovery is the demonstration that S C T and S C A are two related, yet sharply distinct, entities The two conditions do not merge but can be differentiated by genetical analysis (Neel 1949) as well as by the amount of the responsible abnormal hæmoglobin component (Pauling et al 1949) This discovery has considerable clinical interest because in previous years the point of view that every sickle-cell carrier was a possible candidate for S C A found rather widespread acceptance (Beet 1947) This older concept must now be abandoned If we can exclude with certainty the existence of S C A in a person whose erythrocytes are capable of sickling, we can feel assured that this red cell anomaly will not influence his later life On the contrary, once S C A has developed, it will never revert to the inoffensive S C T It follows from this entirely new concept that there is an urgent need for simple and reliable diagnostic criteria to differentiate between the two conditions This is esp true in tropical Africa, where S C T is often grafted on to anæmias of other origin and eve may be masked by some other blood disturba the absence of rigid criteria some doctors will find S C A as often as a patient with sickle cells superimposed anæmia, while others, more cautio ascribe to malaria or to hookworms what is n true S C A Between these extreme attitudes t room for much confusion and hesitation

We briefly review here the differential criteria monly used, and describe a new method that has very useful in our laboratory in distinguishing S C A and S C T

Present Status of Differential Diagnosis

Foy and Kondi (1951) have enumerated very ten methods for differentiating between the ana the trait Seven of these methods, however, are ticable under field conditions in Africa working wit laboratory facilities

Four of the suggested methods have no chance of being introduced, even in a better than laboratory or general hospital service

(1) *Difference in the electrophoretic pattern of the hæ in the two conditions*

(2) *Study of birefringence* under the polarising m

(3) *Presence of alkali resistant hæmoglobin in S C A* This test, apart from being technically complicated (it the use of a water bath refrigerated at 20°C), presents disadvantages First, it cannot be applied to babies two years of age, owing to the normal presence of resistant fœtal hæmoglobin (Most of our patients belo this age group) Secondly, it is probable, as suggested Neel (1952), that all gradations exist between the encountered in S C A and those observed in trait-carri normal persons Finally, the test lacks specificity, i may be positive in non related blood disorders.

(4) *Difference in the survival time of transfused erythrocytes* Transfusion experiments cannot be regarded as a procedure In babies they can be executed only by h trained specialists

Another method is still in its experimental stage

(5) *The anti S C A rabbit agglutination test* —The pre tion of a specifically absorbed rabbit serum that aggl S C A erythrocytes seems indeed the ideal approach to problem A serum with such properties has been prep Schneider and Levin (1950) but it gives such weak that its use would be of little help under field cond Repeated efforts to prepare a similar reagent have entirely unsuccessful in our hands

The following two points are of real value in the majority of cases, but may be very misleading in

(6) *The different clinical picture in the two condit* Among the children sent to the laboratory with the note "shows all the typical signs of S C A" a few had no cells at all on repeated examinations. The coincident p of the sickle cell trait in such cases would erroneously led to a diagnosis of S C A In consequence, however doxical it may seem, a syndrome with the clinical fea S C A in a patient with sickle cells is not necessarily true S C On the other hand, babies and infants affected with S do not always have clinical symptoms, and we have de several cases while making routine blood examinations other purposes It is our experience that babies ra manifest clinical symptoms of S C A during the fir months of life If we admit, as stated above, that S C A congenital anomaly, genetically determined at birth, we m agree that there is a preclinical stage of the disease, and question can be raised as to whether diagnosis is pos without waiting for gross clinical and hæmatol manifestations

(7) *The failure of S C A to respond to any form of treatment* We agree that there is no lasting treatment for S C A, but does not discount the fact that several of our little pa treated with small repeated transfusions and common portive medication left the wards completely anicteric, satisfactory hæmoglobin levels and normal reticul counts In such cases the passage of time will show that improvement was not definitive, but diagnosis should made on admission and not after a prolonged follow up

he three remaining points in the enumeration of r and Kondi (1951) are of incontestable value in erential diagnosis

) *The lower percentage of sickling that occurs in S C A at ced pressures in the Thunberg tube*—This test has been lied by Sherman (1940) to a few cases with very clear-cut ults. Recently however Lange et al (1951) repeated the erimental work of Sherman under better-controlled litions and reached the conclusion that the sharp differen ion between cells from the anæmia and the trait could not ays be made by this technique alone The same over ping of results occurs in the determination of the degree of ling in vivo using the anaerobic venepuncture method rman 1940) Results obtained by these techniques are y significant when they fall into two extreme categories ermediate values are occasionally recorded which require eful interpretation

9) *The presence of sickle cells in stained films of the peripheral d in the anæmic state*—It is well known that sickle cells 17 be present in the stained dry smears of patients with A., despite the inevitable exposure of the blood to atmos ric oxygen (Diggs and Bibb 1939) They are never seen he trait condition; their presence is therefore a simple safe criterion of S.C.A. These "irreversibly sickled cells also recognisable on *immediate* examination of a wet paration of finger prick or venous blood Unhappily this is not constant, and in some cases repeated examination fail to detect a single "irreversibly" sickled cell

10) *The appearance of long filamentous processes in S C A r twelve hours' incubation at 37°C and their absence in the t condition*—We have checked this test in 150 cases of A and several hundred people with the trait and we nd it an extremely reliable tool for differential diagnosis tle cells of the filamentous type were found in all our cases C.A immediately on admission, and a tentative diagnosis ld have been made on this ground alone (Vandepitte 1952 ndepitte and Pieters 1952) American workers independently hed the same conclusion as Foy and Kondi (Neel 1951) filamentous aspect, however is less obvious during the escent periods of the disease and may be entirely obscured repeated transfusions Furthermore this sign may be ative for several weeks or months after birth when only nall percentage of red cells can be induced to sickle even other methods involving the use of strong reducing agents. me of our babies we saw the reversal from the "compact" the "filamentous type of sickling at about the age of months At that time a moderate anæmia was the only ptom, but the diagnosis of S C.A was evident from other thods Another drawback of this method is that trait cells patients with anæmia of other origin, particularly of the ochromic type may also tend to form numerous but finer d shorter appendages Considerable experience and several preparations may be necessary to clarify the diagnosis.

The enumeration of Foy and Kondi (1951) takes no ount of the corroborative evidence offered by the nonstration of sickle cells in both parents. As S C.A. now considered as a homozygous condition it cannot at when one of the parents lacks the sickle-cell omaly It must, however be realised that a few ceptions to this rule can occur: other hæmoglobin omalies—e.g Cooley's trait and the newly described æmoglobin III'—genetically combined with S C T y produce a mild form of hæmolytic anæmia closely nulating S C.A. The present status of this interesting blem has been reviewed by Neel (1952) In our 150 es of S C A only one mother was negative for sickle ls. More exceptions were found among the fathers, t in most instances it was easy to show that the legal her was not the biological father In conclusion, S C.A. very unlikely in a patient whose mother shows no kling when a reliable technique is used

From this brief and incomplete discussion of diagnostic ssibilities it is clear that the doctor in Central rica must rely on careful clinical and hæmatological servations and the results of the last two methods. is combination gave us a clear-cut answer in the at majority of cases Difficulties were, however met very young babies with subtle symptomatology in tients admitted between hæmolytic attacks and in patients who had recently received a blood transfusion In these cases the laboratory data may often be summarised as follows "no sickle cells on the dry smear sickling of an elongated but not typically filamentous type in the moist-chamber method moderate anæmia without icterus; reticulocyte-count slightly raised and occasional nucleated erythrocytes in the peripheral blood" It is in such equivocal cases that a simple and more sensitive test applicable under primitive conditions, is needed for exact differential diagnosis.

New Test Using Bone marrow

As the presence of irreversibly sickled erythrocytes (I.S.E) is the simplest and most specific criterion for the diagnosis of S C.A., we hoped that large numbers of such cells would be found in the bone marrow even when they were not observed in the dry smear or on immediate scrutiny of a wet preparation of the peripheral blood Our hope seemed warranted by previous observations:

Diggs and Bibb (1939) reported 3 patients who had no sickled forms in the dry smears of their blood yet had typical sickle cells which would not become round on exposure to air in their pleural or ascitic fluid

Shen et al (1949) proved experimentally that the persistently sickled form had been assumed because of prolonged or repeated intermittent exposure to anoxia in the capillaries of various organs

The bone marrow with its slow circulation and high oxygen uptake, combines ideal conditions for the production of I.S.E and offers the unique advantage of easy accessibility Moreover we were interested in determining whether the distinction between the "compact" and filamentous' types of sickling would not be sharper when the blood withdrawn with the marrow was examined as a sealed moist preparation

A preliminary trial was made on 2 children with well established S C.A. marrow was taken by tibial puncture and wet sealed preparations were made between slide and cover slip and examined without delay under the dry high power objective of the microscope 2 children with the combination of S C T and anæmia of other origin served as controls. Our first impressions were rather deceptive the marrow with its high content of young and actively growing cells acted as a strong reducing agent on the red blood cells and, when preparations were inspected a few minutes after the marrow had been aspirated a variable degree of sickling was already apparent, even if the patient had only S C.T This rendered it very difficult to recognise with certainty a pre-existing sickle cell among the forms that sickled as a result of the rapid exhaustion of free oxygen from the preparation. Here as in the blood, only the sickle cells of S C.A formed the long filamentous processes after sufficient incubation. The aspect of sickle cells in the S C.T marrow did not differ from that observed in the peripheral blood of the same patient. The distinction between the two types of sickling was in no way more clear-cut than in preparations of the peripheral blood

This trial was almost abandoned, when we were suddenly struck by a bizarre picture found in a small grain of myeloid tissue from 1 of the patients with S C A Several microscopical fields were occupied by an irregular entanglement of numerous rod like structures showing the same refraction colour and transparency as the sickle cells. The whole looked somewhat like a dense mycelium which had been artificially broken into smaller branches 1–3 μ wide of various forms and lengths The individual elements varied from bits of a few microns to filaments as long as 50 μ. Vacuolated areas and fusiform swellings were noted Most of the rods were definitely incurved and seemed to follow the contours of the marrow-cells between which they were inserted Others were sharply bent at various angles like broken matches Fig 1 displays these characteristics A closer examination of the preparations from the 2 S C A. patients revealed

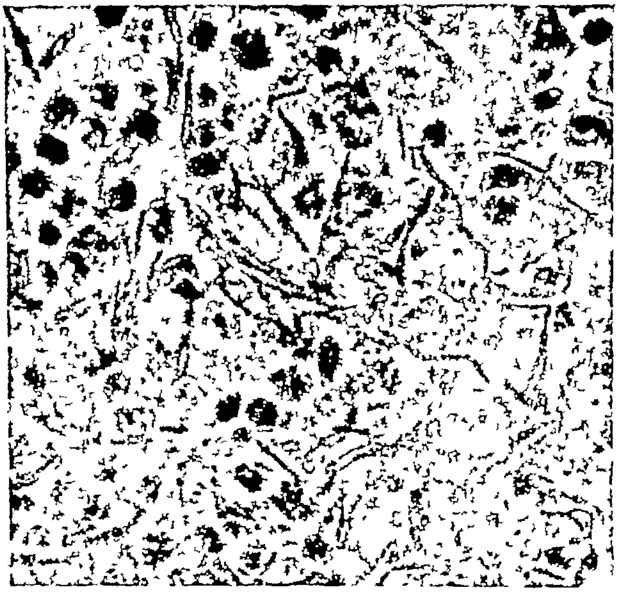

Fig 1—Wet preparation of freshly aspirated marrow from a child with sickle-cell anæmia. Note mycelium like arrangement of hæmoglobin filaments.

other marrow particles containing identical structures Between these particles, in the areas where adult erythrocytes far outnumbered the scattered nucleated cells, some rare rods could be seen floating freely between the cells Their number increased significantly in the neighbourhood of the marrow particles, giving the impression that they had been detached or broken off from the mycelium-like masses in the course of diverse manipulations The morphology of isolated and grouped filaments was not visibly influenced by incubation of the sealed preparation, and the filaments remained unaffected by the progress of sickling No such structures were discovered in the preparations of the controls, even after long examination

The study of the wet marrow film disclosed such neat differences between S C A and S C T subjects that further trials seemed justified We had to verify whether marrow puncture could be introduced as a routine procedure for differential diagnosis between the two conditions

TECHNIQUE

In babies and infants a little marrow, variably diluted with blood, was aspirated by puncture of the proximal end of the tibia In older persons the sternum was preferred The marrow fluid was expelled on to a microscope slide or a watch glass With the edge of a cover slip the solid marrow particles were carefully selected and transferred to a clean slide By a gentle slipping movement the material was spread between slide and cover glass, on which pressure was momentarily exerted to extrude excess blood and to produce a marrow film sufficiently thin to permit satisfactory examination The preparations were sealed with melted paraffin and immediately inspected under the dry high power objective At least three wet preparations were made in this manner for each patient

The "wet marrow test" was reported as ++ positive when one or more of the above described masses of filaments were noted, + positive when only occasional hæmoglobin rods were found scattered among the erythrocytes or enclosed in a marrow grain, and negative when no such structures were detected in the three wet films All the persons included in this study were also subjected to the following examinations erythrocytes and leucocytes per c mm, hæmoglobin g per 100 ml, and differential leucocyte, nucleated red-cell, reticulocyte counts When venepuncture was the percentage of in-vivo sickling and the serum [illegible] level were determined

MATERIAL

We studied 44 patients classified, for convenience four categories

Group I consisted of 15 patients in whom the disease active S C A was firmly established All were [illegible] and showed a frank filamentous type of sickling 6 of had typical sickle cells on a Giemsa stained dry smear ages ranged from two months to seventeen years [illegible] recently been admitted to the hospital and had never transfused

Group II was composed of 12 patients having S.C.T imposed upon another anæmia 2 of them were adu[illegible] megaloblastic marrow picture, and the remainder infants with a hypochromic anæmia due to [illegible] infestation and/or malaria

Group III contained 12 patients in whom S C.A had diagnosed on admission During a period of at least weeks they had been *transfused repeatedly* with comp blood and had also received parenteral liver, folic acid, B_{12}, and iron Under this therapy the characteristic logical features of S C A had been masked to various de filamentous sickling was discrete and sometimes diff discern

Group IV consisted of 5 siblings of S C A patients were not considered ill by their parents, but their pictures showed various signs suggesting S C A [illegible] anæmia with polychromatophilia, increased reticulocyte leucocyte counts, and a tendency to the filamentous ty sickling The preclinical stage of S C.A was therefore suspected

RESULTS

The results of the marrow examination are summa in the accompanying table In the patients with

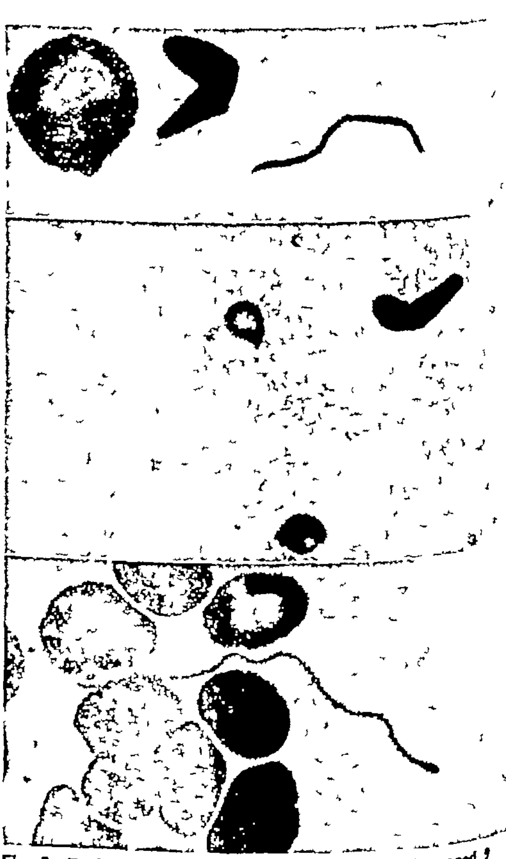

Fig 2—Eosin-stained thin blood-smear from baby aged with sickle-cell anæmia. Note mechanical fragmentatio irreversibly sickled red cells.

RESULTS OF WET MARROW TEST IN 44 PATIENTS

Group	No of patients tested	Wet marrow test			No. of patients with sickle cells on dry smear
		+ +	+	–	
tive S.C.A	15	13	2	0	6
C.T with other anæmia	12	0	0	12	0
reated S.C.A	12	10	0	2	4
reclinical S.C.A	5	5	0	0	0

A a positive wet marrow test was always found ther with the filamentous type of sickling in the pheral blood Differences in the aspect of the sickle , however are to some degree quantitative and a ter of subjective appreciation Therefore it is easily erstood that a more quantitative test, giving a r-cut all or none result, will be preferred by the less erienced worker The new wet marrow test fulfils demand Neither age nor sex of the patient, nor the rity of the anæmia, seemed to influence the degree ositivity of the marrow picture A strongly positive was noted in a patient with a red-cell count of more 1 4 000,000 yet showing the typical joint pains of On the other hand, the 2 weakly positive results table) were observed in very anæmic patients. The results were obtained when large and numerous row particles could be aspirated and inspected It be worthy of note that a strongly positive wet row test was obtained from the 1 S.C.A patient in series whose mother was a non sickler Also in other ects there was no reason to admit that this case was severe than the classical S.C.A as seen in homozygous ects. The question therefore remains open whether patient was heterozygous or, as a result of mutation ozygous for his sickle-cell gene

ur work emphasises the difficulty met with in nosing S.C.A in patients who have been recently and atedly transfused Of the 12 S.C.A patients belonging his category only 5 exhibited typical filamentous le cells the remainder giving equivocal readings, after prolonged incubation of the wet blood film examination of the wet marrow aspirate produced lence of S.C.A. in 10 of those cases. In the 2 others, e of the hæmatological findings pointed towards the ibility of S.C.A although its existence had been ly established a few weeks before Such diagnostic culties are only avoidable when every Negro patient, spective of his complaints, is screened for the sickling lency of his blood within the first hours of his hospital ission

he superiority of the wet marrow test was best ealed by its application to children with preclinical The youngest patient in this group was only n weeks old and apparently in perfect health It be interesting to apply the new method to younger les and it is conceivable that positive results will be d in the newborn S.C.A may also exist in a latent n in older children; a positive wet marrow test was d in an apparently normal girl of more than five rs Her blood picture, however was compatible with existence of a well-compensated anæmia of the nolytic type

Discussion

he microscopical picture offered by a positive wet row test is so conspicuous and so impressive that one wonder that it has not been described before. This t chiefly be attributed to the failure of previous kers to examine wet films of their marrow aspirates. have found one published reference of such examina but only the enhancement of the sickling progress noted (Singer and Robin 1948) Although dozens of kers have examined stained dry marrow films of their A patients only very few noted abnormalities that ht be related to the impressive picture regularly observable in wet specimens In several bone-marrow smears from patients with S.C.A Wintrobe (1951) saw some very long filamentous bands of what appeared to him erythrocyte cytoplasm Many years before him Sydenstricker et al (1923) had made the same discovery on necropsy material of a child with S.C.A. We had no difficulty in finding the same filaments in the *stained* marrow smears of our cases; but they were never so conspicuous as in the wet film and it was exceptional to find two or three of them together in the same microscopical field The enormous advantage of the wet marrow film for diagnosis can be easily explained on purely technical grounds The quantity of marrow aspirate necessary for a dry film is only a minute fraction of what can be rapidly inspected in a wet preparation In addition the delicate mycelium like arrangement of the hæmoglobin filaments is disrupted in spreading the film, and only widely scattered and rather amorphous debris is left.

Although our work was primarily undertaken to demonstrate a new diagnostic difference between anæmia *and trait cells, our findings also shed new light on the* disintegration of red cells in S.C.A A few years ago no satisfactory explanation could be given for the difference between the survival time of anæmia and trait erythrocytes Some workers found it conceivable that an additional structural alteration different from the sickling tendency might be operating in the production of S.C.A (Singer et al. 1948) We have now additional evidence that the different behaviour of trait and anæmia erythrocytes can be satisfactorily explained by the morphological differences in their actual sickle shape It has been repeatedly emphasised that only a very small percentage of trait cells assume the sickle shape within the circulation and as those sickle cells are only slightly incurved and not significantly elongated it is admissible that their mechanical *fragility in vivo remains* unaltered Disintegration of trait cells is therefore not accelerated beyond the normal rhythm of erythrocyte decay By contrast in patients with S.C.A an important proportion of erythrocytes circulate in the sickled form and as they carry about a double dose of the abnormal hæmoglobin they take on a definitely elongated crescent shape and develop long rigid processes These brittle needle like filaments are continuously broken off during the passage in the narrow capillaries of different organs. Fig 2 shows successive phases of the mechanical erythrocyte disintegration seen in the peripheral blood of a nine-week-old baby with severe S.C.A

Our findings in the marrow of S.C.A patients reinforce the opinion that mechanical factors have a preponderant rôle in the pathogenesis of the hæmolytic process. When sickle cells of the filamentous type pass through the venous sinusoids of the bone marrow their sharply pointed ends may slip through the small openings between the lining cells of the endothelial wall Once they have left the vascular bed these erythrocytes are caught in the interstices of the marrow stroma where they cannot be perfused out. In this highly cellular environment the abnormal hæmoglobin is further reduced and undergoes a maximal crystallisation provoking the extreme and irreversible deformations of the red blood-cells. The ultimate fate of these trapped hæmoglobin bands is probably lysis and phagocytosis. More information on their exact localisation will probably be provided by serial sections of fixed bone marrow Our hypothesis could further be tested by transfusing massive doses *of S.C.A blood into normal recipients. If our inter*pretation is correct the abnormally short survival time of the transfused red blood-cells should be reflected by the appearance in the recipient's marrow of the typical hæmoglobin filaments

Our work favours the view that the bone marrow takes a part in the blood destruction of S.C.A although this part may be qualitatively rather unimportant It is, however, probable that the same mechanism of selective filtering and trapping of sickled erythrocytes may be operating in other organs of the reticulo endothelial system

Summary

The differential diagnosis between sickle cell anæmia (S C A.) and anæmia of other origin grafted on to sickle cell trait is of first importance in Central Africa When laboratory facilities are not available, much information can be gained by simple inspection of the stained thin blood-smear, and of the sickle-cells after overnight incubation using the standard moist-chamber method The practical value of the latter method was substantiated by its successful use in over 150 cases of S C A at Leopoldville The test is of limited value in transfused patients and in the preclinical disease

Examination of wet marrow films of S C A patients revealed bizarre formations made up of numerous hæmoglobin filaments These were so constantly absent from the marrow of persons with sickle cell trait that their presence may be accepted as a safe and sensitive criterion of sickle cell anæmia The only failures of this new method were noted in two S C A patients who had received repeated transfusions

Some theoretical implication of these findings are considered, and a mechanical explanation of the blood destruction in S C A is briefly presented

We wish to thank the team of doctors who selected the patients for this study, especially Dr F Périn of the Government Hospital

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PERFORATED DUODENAL ULCER IN CHILDREN

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PEPTIC ulceration in children is relatively uncommon Hutchins (1944) found that only 243 cases of peptic ulceration in infants and children had been reported, and only 77 cases of perforated peptic ulcer 2 further cases of perforated duodenal ulcer are described here

CASE-RECORDS

Case 1 —A boy, aged 5 years, was admitted on July 8, 1952, having had pain in the centre of his abdomen from 5 P.M the previous evening, which had kept him awake during the night He had felt sick but did not vomit On the day of admission the pain had persisted and had spread to the right iliac fossa He had no other symptoms His temperature on admission was 100 4°F

He had been in hospital three months previously with similar but less severe pain, and had been kept under observation for five days He had otherwise bee healthy child, except for influenza at the age of 2½

On examination he was well nourished and lo His tongue was moist and had a greyish white coat glands were palpable in his neck. His abdomen m with respiration There was tenderness in the rig fossa, but no rebound pain was elicited and no felt The tender zone in the right iliac fossa to the level of the anterior superior iliac spine Th no tenderness on rectal examination The both acute appendicitis and mesenteric adenitis.

Operation —With the child under general anæs made a right gridiron incision and found turbid fluid peritoneal cavity The appendix was retrocæcal but normal A few small mesenteric glands were palpable incision was extended upwards and outwards, and indurated area at the pylorus was then easily This was seen to be the site of a chronic duodenal with a small perforation in the centre, partially by adherent omentum, A search was made for a foreign body, but none was found The perforation closed and the omentum oversewn in the usual way area of induration in the first part of the duodenum for about half an inch

Postoperatively the patient made an uneventful and was discharged from hospital twenty two da operation Plain radiography of the abdomen did not any foreign body in the peritoneal cavity A barium showed considerable scarring of the duodenum, of the gastric mucosa, and what appeared to be an the lesser curve of the pars media

Case 2 —A girl, aged 5 years, was admitted to the Hospital for Sick Children on Oct 22, 1945 Her previous illness was measles There had been no dyspeptic symptoms On the day before admission the day of admission she had complained to her "crampy pains in the stomach" She was at school day of admission to hospital, and had vomited once the same evening she was walking along the road w parents, when she vomited again and said that the her stomach was worse About two or three hours she was admitted to hospital Her appetite was good up to the onset of symptoms she had had no urinary and her bowels were regular

On examination she looked healthy Her abdomen but little with respiration, especially the lower part palpation there was rigidity of the lower abdomen, marked on the right side The upper abdomen was rigid nor tender There was tenderness in both iliac more severe in the right On rectal examination slight tenderness on the right side There were no constituents in the urine The child said that the been all over her stomach at first but was now in the side only Acute appendicitis was diagnosed

Operation —With the child under general opened the abdomen through a right-gridiron incision found the appendix normal, but clear free fluid, with fragments of peas, escaped through the wound. incision was extended upwards and a perforation of anterior duodenal wall was found No induration the perforation. The perforation was closed with sutures, and the peritoneal cavity aspirated

Postoperative Course —The patient's general condi good throughout the operation, her temperature 101 8°F on the day after the operation, but subs 99°F in the next twelve hours She made an une recovery and was discharged on the fifteenth day

DISCUSSION

Since Hutchins's (1944) report 13 more cases been collected in the past ten years (Spencer Rogerson 1951) Proctor (1925) found 2 children necropsies in ulcer cases at the Mayo Clinic in 1 Ladd and Gross (1941) have analysed the cases and have drawn the following conclusions

(1) Ulcers are more common in infancy, and least in children aged 2–7 years.

(2) Ulcers in infancy are more likely to bleed and forate, whereas ulcers in later childhood are more perforate and to cause stenosis.

2 present cases seem to be in agreement with the rvation about perforation

no diagnosis of perforated peptic ulcer was not ght of in these cases. Further questioning after the ation did not elicit any definite previous history of r in either case.

he sharp contrast between the 2 present cases and s of perforated peptic ulcer in adults is most inter g In adults generalised abdominal rigidity is usually d in association with severe abdominal pain of len onset In neither of the present cases did the seem severe and there was no generalised rigidity ther case 1 was characteristic of perforation of a nic ulcer, whereas case 2 was characteristic of oration of an acute ulcer

wish to thank Mr Ian Fraser and Mr S M Cohen for ission to publish these cases and Dr J M Corall for the graphic examination.

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A TRAUMATIC HÆMOTHORAX

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ÆMOTHORAX is seldom seen in civilian practice, and n it does occur is usually caused by broken ribs he following case it was an uncommon sequel to a mon accident

CASE RECORD

healthy boy aged 11 was climbing a tree, when he fell ugh the branches about 40 ft to the ground On being ed up he was a little dyspnœic but quite conscious. He taken to a nearby hospital, where he was found to have a rficial laceration of the left lower abdominal wall; he also eared to have fractured lower ribs on the left side one of h was distorting the skin. The laceration was sutured with e stitches and the boy was given anti tetanus serum. to bed, and given penicillin 400 000 units daily

uring the next two days his temperature remained raised 01°F and his left chest became dull to percussion On the d day he was transferred to the County Hospital Hereford er the care of Mr F Brian Thomas.

n admission the laceration in the boy s lower abdomen healing well His apex beat was in the 5th interspace to the right of the sternum and the whole of the left side his chest was dull to percussion I could not confirm the ence of fractured ribs, however and asked for radiographs. o confirmed the presence of fluid with a small apical umothorax but showed no fracture.

reatment and Progress —*Aspiration with a wide-bore needle* duced only a small cylindrical clot, and it was concluded t he must have a coagulated hæmothorax. Penicillin ,000 *units was given six hourly Except for his injections* boy was comfortable though slightly dyspnœic. He was dly pyrexial but otherwise in good condition, and the air ry in his left lung increased a little as the pneumothorax absorbed

On the seventeenth day after the accident the boy com ined of a pain in his back. There was a hot red swelling h a pale fluctuant centre below the angle of the left pula. Deep to this a hard resistance was felt which led to believe that exuberant callus was forming round a viously undetected fracture of a rib Radiography again wed an undamaged thoracic cage and the abscess aspirated. A little pus was obtained and sent for ture but the point of the needle met a harder object When agment of skin was removed over the centre of the abscess, oreign body resembling a small spicule of wood was seen. ing to the surrounding inflammation and the hæmothorax ther local nor inhalation anæsthesia seemed suitable for its oval A poultice was applied with a protective ring sing to keep pressure from the site No scar was found on chest through which the wooden splinter if such it were, ld have entered

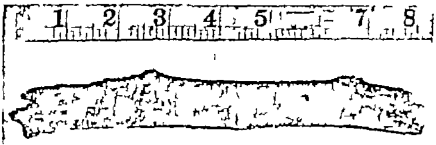


Fig 1—Broken stick of cherry wood $8^1/_2$ in. long and 1 in. in diameter which entered patient's thorax.

Next day the pus was reported to contain *Clostridium welchii* (later proved to be penicillin sensitive) and coliform bacilli

Removal of Foreign Body —Mr Brian Thomas inspected the abscess, which now showed quite clearly a fragment of wood He applied a stout pair of forceps to its end and with a steady pull extracted a broken stick of cherry wood $8^1/_2$ in. long and 1 in in diameter (fig 1)

Subsequent Progress —The patient said he felt much better for this operation, which was at once followed by a slight sucking pneumothorax controlled by a large wet pack. *During the next three days a large amount of serous exudate* drained from the thorax, and the boy recovered steadily Radiography now showed good re-expansion in the left lung and for the first time a visible track rising from the apex of the tented left dia phragm (fig 2) The wound in the back con tinued for some time longer to discharge small quantities of serous exudate in which a piece of check shirt material and a fragment of flannel trouser were found. The patient made an uninterrupted recovery in hos pital the re expansion of his lung being en couraged by seg mental breathing exercises He remained up and about during *this period and on one* occasion he tracked me to my room demanding to see his stick He looked at it for a minute exclaimed Coo what a whopper! *and was gone delighted*

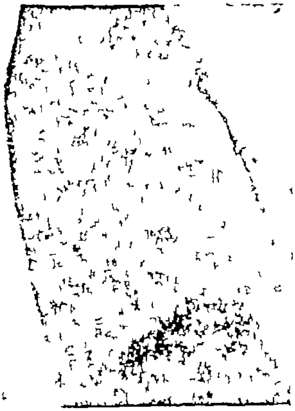


Fig 2—Radiograph of left lung soon after removal of foreign body

Follow up —Three months after discharge from hospital he was in excellent health, with a healed chest wound and radiologically normal lung and diaphragm and was playing football for his school

CONCLUSIONS

The only wound on admission was the linear laceration $2^1/_2$ in long in the anterior abdominal wall, level with the anterior superior iliac spine and 1 in. to the left of the midline The piece of wood must have entered here traversed the abdomen missing intestine stomach and spleen to perforate the *left dome of the diaphragm* It must then have transfixed the left lung missing the heart, and presented between the sixth and seventh ribs posteriorly mimicking a fractured rib, though no rib was damaged

The *Cl welchii* responsible for the infection was still alive after seventeen days' treatment with penicillin, to which it was sensitive Little of the antibiotic may have reached the centre of the hæmothorax, and the coliforms present may have inactivated that which did

The infection was responsible for the clotting of the hæmothorax

The wood must have had exactly the same radiotranslucency as blood, since the most careful subsequent scrutiny failed to show its presence in the chest radiographs

The young human organism possesses remarkable resilience to even dramatic traumata of bacterial, dynamic, and structural types

SUMMARY

A piece of wood $8^1/_2$ in long and 1 in in diameter passed through a boy's abdomen into the left side of his thorax without damaging any abdominal viscus, the heart, or ribs The boy recovered completely after the stick had been removed

I am indebted to Dr Cameron Gibson who first attended this patient, and to Mr F Brian Thomas, under whose care he was at the County Hospital, Hereford, for permission to publish

Preliminary Communication

INFLUENCE OF PHENYLALANINE INTAKE ON PHENYLKETONURIA

In phenylketonuria phenylalanine accumulates in the blood and cerebrospinal fluid, probably because phenylalanine is not converted to a normal extent into tyrosine On the assumption that this excessive concentration of phenylalanine (or perhaps of some breakdown product) is responsible for the mental retardation found in this condition we decided to keep a girl, aged 2 years, with phenylketonuria on a diet low in phenylalanine She was an idiot and unable to stand, walk, or talk, she showed no interest in her food or surroundings, and spent her time groaning crying, and banging her head The diet had to be specially prepared, because a sufficiently low phenylalanine intake could only be attained by restricting practically all the nitrogen intake to a special casein (acid) hydrolysate (Allen & Hanburys Ltd) This was treated with activated acid-washed charcoal, which removed phenylalanine and tyrosine Tyrosine, tryptophane, and cystine were then added in suitable amounts

RESPONSE TO LOW-PHENYLALANINE DIET

The child was at first treated in hospital so that careful observation could be made During a four-week preliminary period, when no phenylalanine was permitted, no definite clinical change other than loss of weight was observed The characteristic musty smell disappeared, the levels of phenylalanine in plasma and urine fell to normal, the excretion of phenylpyruvic acid ceased, and the ferric chloride reaction became negative (see figure)

Subsequently, presumably as the result of tissue breakdown, the biochemical abnormalities returned to some extent, along with a generalised amino aciduria Phenylalanine was therefore added in small amounts in the form of whole milk, a daily intake of 0 3-0 5 g being found sufficient for normal weight gain with greatly improved biochemical findings

During continued outpatient treatment a improvement in the child's mental state took within the next few months she learnt to crawl, and to climb on chairs, her eyes became bright hair grew darker, and she no longer banged her or cried continuously

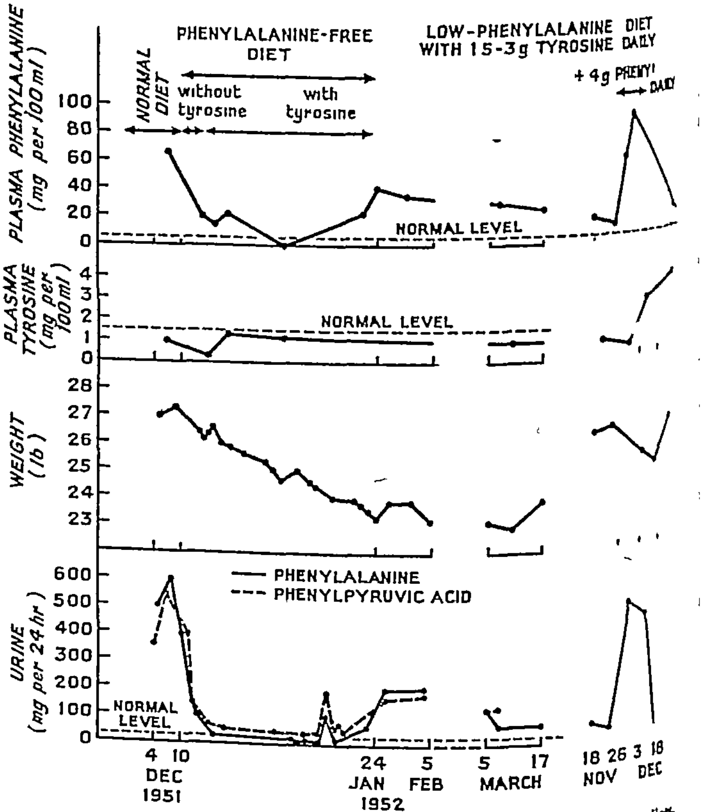
The most suitable diet so far evolved conta source of amino acids only the special hy vegetables and fruit, gluten-free bread and flour freely permitted

RESPONSE TO ADDITIONAL PHENYLALANINE IN

In view of the importance of establishing the clinical improvement noted (which depend first largely on the observation of the mother) w and due to the diet rather than to natural develo we decided to add L phenylalanine 5 g daily t diet This was added to the hydrolysate without mother's knowledge, so that any change shoul noted without bias

A definite deterioration in the child's condition the mother reporting with distress that her d had lost in a few days all the ground gained previous ten months, that within six hours of the fresh supply of "food" the child had begun and to bang her head as in the past, and within four hours could no longer stand and could crawl

In view of the importance of obtaining ad proof of the value of the special diet, at present



Biochemical reactions to phenylalanine-free and to low-phenylalanine diet

expensive, the mother agreed to a further similar in hospital, which permitted close correlation of c and biochemical findings and cinematographic r After a period of observation on a low phenyl diet, L phenylalanine 4 g daily was again added to diet Within twenty-four hours the patient b irritable and drowsy, lost interest in her food oundings, developed facial eczema, and salivated fusely She also became ataxic and vomited repeat- By the sixth day she could no longer stand or The additional phenylalanine was then discon ed and within three weeks she had almost completely vered.

BIOCHEMICAL FINDINGS

Vhen phenylalanine was added to the diet, the ma phenylalanine level rose from 13 to 91 mg per ml, and the urinary excretion of this amino acid eased from 40 to 500 mg per 24 hr (see figure and le) Two weeks after the extra phenylalanine had n discontinued the urinary excretion of this amino d decreased *to 20 mg per 24 hr and the plasma* nylalanine level fell during the next few weeks to and then to 19 5 mg per 100 ml, and is now normal mg per 100 ml) The ferric-chloride test, which negative with the low phenylalanine diet gave lack green reaction while the child was receiving a phenylalanine

NYLALANINE AND TYROSINE LEVELS IN A PHENYLKETO URIC PATIENT AND IN A CONTROL BEFORE AND DURING PHENYLALANINE FEEDING EXPERIMENT

—	Phenylketonuric patient		Normal control	
	Phenyl alanine	Tyrosine	Phenyl alanine	Tyrosine
plasma (mg per 100 ml)				
fore phenylalanine feeding	13·0	0 7	1 1	1 7
uring feeding of L-phenylalanine 4 g daily	90 5	·7	6 1	2 0
rine (mg per 24 hr)				
fore phenylalanine feeding	40	5 3	4 2	6 4
uring feeding of L-phenylalanine 4 g daily	500	14 0	[illegible]00	11 0

On a diet low in phenylalanine.

Ve have also given phenylalanine (14 g in four days) normal infant, aged 5 months, without producing change in behaviour or any comparable rise in the ma phenylalanine level which did not exceed 6 1 mg 100 ml. (see table)

hese findings suggest that high levels of phenylalanine of its breakdown products disturb cerebral functions may possibly give rise to the mental retardation found henylketonurics

CONCLUSION

n this child at least the beneficial effects of a low nylalanine intake seem unequivocal although the ree of mental development finally obtained remains be seen after further prolonged treatment. In view he importance of phenylketonuria as a cause of mental ciency further controlled trials are being made, cial attention being paid to very young children, who likely to benefit most.

Ve gratefully acknowledge the help and interest of Dr O. Smallwood Prof J M. Smellie and Prof J R dre Dr L. I Woolf first drew our attention to the nique of removing phenylalanine from casein hydrolysate gave further valuable assistance Messrs Allen & burys Ltd have recently presented us with a supply of nylalanine free casein hydrolysate

he methods employed will be described in a fuller account o published in *Acta pædiatrica*

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* In receipt of a grant from the Medical Research Council

Reviews of Books

William Cheselden, 1688–1752

SIR ZACHARY COPE, M.D M.S., F R.C.S., consulting surgeon St Mary s Hospital London Edinburgh: E & S Livingstone 1953 Pp 112 20s.

Cheselden was the foremost surgeon of his time and in this lively and well illustrated book Sir Zachary Cope has provided him with a worthy biography

Cheselden retired from the staff of St Thomas s Hospital before Percival Pott was elected to the staff of St Bartholomew's Hospital His general surgical ability was great his ophthalmic work enterprising and in some respects original and his speed and success in cutting for the stone had no equal *in pre-anæsthetic days. But he achieved something* more than this and something greater and more lasting for his technical skill died with him He was the first man in this country who insisted on the importance of a sound knowledge of anatomy for the medical student and upon dissection for a knowledge of anatomy He was the first regular and recognised teacher of anatomy in Great Britain There had indeed been courses of anatomy before his time but none which continued regularly with a printed syllabus and a companion textbook which became so popular that it maintained its place for more than a century

Sir Zachary shows him in many guises. We are shown the lithotomist gradually evolving his own technique. We see him as the architect of the old Fulham (or Putney) Bridge—a wooden memorial which withstood heavy traffic for 150 years. We see him as a teacher instructing among others, John Hunter We see him as a superb draughtsman his *Osteographia* has lived because of the beauty and accuracy of the pictures he drew for its text was far less satisfying We see him as a negotiator responsible more than anyone else for separating the Surgeons from the Barbers

British Medical Science and Practice

An anthology Editor: G F PETRIE M D London: Longmans, Green 1953 Pp 172 15s

THIS anthology has been sponsored by the British Council with the object of helping doctors and students abroad to follow modern trends of medicine as it is practised in Britain It might be thought that such a compilation would be scrappy but this interesting and impressive collection well illustrated well printed and well arranged is a credit to its editor and publishers.

The introductory section briefly surveys some of the landmarks in British medical history as illustrated in the work of ten pioneers—Harvey Hunter Jenner Bell Bright Addison Simpson, Florence Nightingale Lister and Manson. The character of each is portrayed through excerpts taken from their own writings and from standard biographies. The small selection of aphorisms ranges from the 17th to the 20th centuries. The only living contributor Geoffrey Keynes holds his own in distinguished company with three apt aphorisms—for example Speed in a surgical operation depends not on quick movements but on the absence of unnecessary movements. The third and main part of the anthology deals with present-day medical science and rightly fills three-quarters of the book Extracts of up to 500 words have been chosen from articles by distinguished authorities in almost every branch of medicine An appendix gives the qualifications and experience of the contributors

Ciba Foundation Colloquia on Endocrinology

Vol 6. *Hormonal factors in carbohydrate metabolism* Editor: G E. W WOLSTENHOLME, O.B.E. M.A M.B assisted by JESSIE S FREEMAN London: J & A. Churchill 1953 Pp 350 35s

MOST of us have had trouble with the management of diabetes and our difficulties are not all explained by poor coöperation from the patient; nor will they all be resolved by newer types of insulin This engaging volume shows why each diabetic is an individual problem It plunges straight into a discussion of alternative pathways of carbohydrate oxidation and thence into localisation of enzyme systems in the liver cell; after which, Dr C H Best F R.S the chairman was driven to exclaim I d like to bring the clinicians into this discussion but I don t know just how to do it." Important papers follow on the interconversion of carbohydrate, protein, and fat, and the influence of pituitary and adrenal hormones on the disposal of ingested carbohydrate These are more obviously related to clinical problems—though the fundamental issues raised in the first group of papers may affect them more decisively in the end The influence of insulin on carbohydrate metabolism is discussed in six papers, one reviewing the evidence that the first action of insulin on carbohydrate metabolism is to facilitate the entrance of extracellular glucose into the cell, with its enzyme systems Finally there are papers on sex hormones, pregnancy, and carbohydrate metabolism

Reports of many conferences give the impression that while those who attended enjoyed a stimulating experience, their deliberations, set down in cold print, hardly deserve permanent record This particular conference was an exception, certainly from a clinician's viewpoint For those unused to enzyme chemistry spoken discussion of the fundamental problems must have been difficult to follow, but in print, to be read at leisure, they at least begin to be comprehensible, and to show some relevance to the spuriously simple problems of clinical diabetes This is just the book to quicken an interest—which has perhaps been dulled by an unending procession of patients—in the mechanism of this fascinating disease

Juvenile Delinquency

J D W PEARCE, M.A, M D, F R C P E, D.P M, physician in charge, department of psychiatry, St Mary's Hospital, London London Cassell 1952 Pp 396 25*s*

THIS book, surveying the whole field of juvenile delinquency, is written for magistrates, probation officers, and other non-medical readers as well as for doctors

Such a broad approach handicaps the author Thus the magistrate will find the section on law too elementary, while the psychiatrist will have a similar criticism of the account of child development Nevertheless Dr Pearce has been fair in his emphasis and he says something to interest everybody The reader who comes completely fresh to the subject may be confused by the many different aspects, especially as they are not always dealt with in sequence Thus we have two pages on "instincts" while the development and modification of instinctual urges is discussed twenty pages later, and the relationship between these instincts and delinquency is considered thirty pages earlier It may of course be argued that delinquency can be studied from so many aspects that a consistent approach is one sided, so whether Dr Pearce's presentation seems commendable or not will depend on personal predilection

This is not a vivid book, but it is honest, unemotional, and comprehensive Although the reader will not be inspired, he will not be misled

Sulphonamides and Antibiotics in Man and Animals

2nd ed J STEWART LAWRENCE, M D Edin, M.R C.P, lecturer, department of occupational health, JOHN FRANCIS, M SC, M R C V S, professor of preventive medicine, University of Queensland Veterinary School, with the assistance of ARNOLD SORSBY, M D, F.R.C S, research professor in ophthalmology, Royal College of Surgeons, and PHILIP G SCOTT, F.R C S, consulting surgeon, E.N T department, Royal Devon and Exeter Hospital London H K Lewis 1953 Pp 482 42*s*

WHEN the first edition appeared seven years ago the only established antibacterial drugs were the sulphonamides Penicillin was still restricted to hospitals, and the other antibiotics now in use were still in the laboratory stage or unknown The new edition includes the sulphonamides, the antibiotics, the sulphones, the thiosemicarbazones, *p* aminosalicylic acid, and isoniazid As in the first edition, the emphasis is mainly on clinical aspects The first part deals with mode of action, chemistry, bacteriology, pharmacology and toxicology, drug resistance and choice of drug in treating a specific infection Then comes a brief description of each drug, followed by the treatment of diseases due to infection, which are classified bacteriologically and regionally The chapters dealing with the veterinary use of antibacterial agents are written by Professor Francis.

This book is intended for the medical or veterinary practitioner who needs a brief, practical, and up-to-date exposition of the subject and it well fulfils this function

Conquest of Plague

A Study of the Evolution of Epidemiology L FABI M D Lond Oxford Clarendon Press 1953. P 42*s*

THIS lengthy book deals, in broad outline, wi age-long evolution of conceptions of the nature of p It ends with a brief account of those recent dis which have at last enabled man, not only to p himself against this most ancient and formid epidemic diseases, but even to cure most of the v It is not a history of plague epidemics nor a sy textbook, but a study of the development of t beliefs about the origin of the malady from th primitive man to the present day

The book is divided into four parts The first des traditional conceptions of the disease The second the work of modern research workers on the nature of The third discusses the effect of the local and distribution of the chief species of rat-fleas upon th of bubonic plague, and the fourth deals with nation international measures of plague prevention Wit discovery of pesticides, sulpha drugs, and antibiotic no longer too optimistic to speak of the conquest o disease The mortality of Indian cases of moderate has been reduced from 75% to 10% or less.

Dr Hirst has an international reputation for into the epidemiology of plague and he has studied disease and its history for fifty years He has an important and well-documented monograph he regards as only an introduction to the subject.

Enzymatic Concept of Anaphylaxis and Allergy

Z Z GODLOWSKI, M D Cracow, PH D Edin. research fellow of the Carnegie Trust, Edi Edinburgh and London. E & S Livingstone. Pp 120 15*s*

IN attempting to formulate an enzymatic conc allergy and anaphylaxis Dr Godlowski has drawn diverse sources which are often difficult to relate to other

In this, and in the deductions from his own ex he has permitted his theoretical concept to colour his pretation of the findings For example, he claims that e phil leucocyte cells can develop, as a result of the changes, not only from myeloid tissue but also from int epithelial cells, whence they migrate into the deeper The opposite possibility, that the eosinophil cells migrated from the blood vessels into the subepithelial epithelial tissues, he dismisses as highly improbable, due consideration of the histological pitfalls which ca from the superimposition of eosinophil granules on othe and from the changing appearance of amœboid m cells due to the pressure of surrounding tissue cells.

In his foreword Professor Drennan disarms cr by admitting that "it may be objected that th more theorising than the facts merit" But Godlowski's colleagues will be stimulated by his ing experiments on the influence of antigenic and d genised diets on circulating and tissue eosinophils on the influence of heparin and cortisone on eos and other white blood-cells

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Insecticides (H.M Stationery Office 1953 £3)—The committee on insecticides of the World Health Org had the task of establishing specifications for inse to be used against vectors of disease in man, and for spr equipment used in malaria control This strongly b loose leaf volume contains all the specifications esta by the committee in the last four years, and it will be convenience for users of these products, as well as f manufacturers, to have them gathered together in thi Some dozen products are listed here, and there are specifications for spraying and dusting apparatus A include a guide to sampling procedure, weights and and a list of members of the expert committee, and are some 20 pages for notes Additions and amen can be added to the book as they are published, th be forwarded on request to holders of the volume, th of this service being included in the original purchase

THE LANCET

LONDON SATURDAY OCT 17, 1953

The Drug Bill

N the past few years doctors have had less cause n formerly to consider the economics of prescribing far fewer patients have been paying for their dicines Furthermore prices have seldom been ntioned in pharmaceutical advertisements in medical rnals—a policy related apparently, to differences price when the products are sold abroad Before late war panel practitioners were kept informed the cost of their prescribing as compared with the a average, but this practice has not proved sible under the National Health Service owing to delay in pricing occasioned by the vast numbers prescriptions. Yet the need for such information greater than ever before The steady rise in the ion's medicine bill has caused great concern to Ministry of Health, and last week the Minister nted out (see page 820) that the current rate of enditure under this head (£46 300,000 per annum) *prejudicing other urgent developments.*

Whereas at the start of the National Health Service prietary preparations accounted for 24% of the al ingredient cost, in 1952 they accounted for 56% e Ministry has now issued two lists giving the t of some commonly used proprietary preparations d of some *National Formulary* preparations In ny instances the cost of the proprietary preparation ompared with that of the official equivalent, (in cases the prices for the latter include ingredients cost allowance dispensing fee, and container allow ce) Of the 243 proprietary preparations listed the t, compared with that of the equivalent standard paration, is higher in 67 lower in 47 and the same 10, for the remainder no equivalent standard paration is named The proprietary preparations ich are lower in price than the standard drugs lude certain sulphonamides, barbiturates, vitamins, d sex hormones These figures should dispel the pression that nearly all proprietary preparations needlessly expensive and clearly the practitioner n continue to prescribe some well tried proprietary parations without misgiving Though this list y lead to some saving from reduced demands for less well established and more expensive prepara ns, the main saving is likely to come from a general vering of costs through healthy competition between oprietary and official drugs

Proprietary preparations remain important to dical practice and the contributions of the main armaceutical firms should receive proper financial ward. These firms have not only done much to luce the gap between laboratory knowledge and erapeutic application but have also contributed bstantially to basic medical as well as pharmaceutical earch Even the development of palatable and convenient preparations is no negligible service to patient and doctor These contributions to medicine are however, somewhat offset by the excessive multiplication of preparations and by the marketing *of many less desirable products* By any standard, some thousands of proprietary remedies is far too many Some have in their time been useful but have been surpassed by more potent drugs, others, of limited value, have had their sales maintained more by the personality of pharmaceutical representatives or by polychromatic bulletins than by any scientific evidence, some have been based on pharmacological misinterpretations, and a few have been complete impositions Hitherto these preparations have had to be assessed by the busy general practitioner without disinterested guidance except from reports in the medical journals Lately however the Cohen Committee[1] has classified five thousand proprietary preparations placing in categories 5 and 6 drugs which they regarded as not proved to be of therapeutic value —which is, of course by no means the same thing as proved not to be of therapeutic value. This classification should result in appreciable saving, by discouraging the use of these less essential preparations and strengthening the practitioner's hand against overdemanding patients He retains his own freedom of action for he may still prescribe whatever drug he wishes, but if there is evidence of excessive prescribing he may be called on to justify his actions to his colleagues on the local medical committee No doubt the committee will most commonly be considering the *prescription of drugs in categories 5 and 6* but, as Mr G D STEWART shows in his retort (p 833) to our comment[2] on a case lately considered in Northern Ireland, heavy prescribing of even well-established preparations may be very expensive The procedure of justifying prescriptions to the local medical committee provides a proper safeguard for the public purse without, we *believe unreasonably impairing* professional freedom At any rate the decision whether individual freedom shall or shall not be restricted rests primarily with a professional body

No measure however can be effective without the practitioner's willing coöperation Much depends on his attitude to prescribing, and on other pages Dr *HANDFIELD-JONES and Dr BARHAM CARTER* make some sensible suggestions on the right line to take towards the prescribing of placebos As regards costs the Ministry has now set about trying to influence the attitude of the oncoming generation of practitioners the Ministry's chief medical officer has lately addressed to clinical teachers a letter asking them to consider whether more *information on the cost of* prescribing can be included in the curriculum This approach, however cannot show immediate results For the present generation of doctors the way could still be made easier For instance the Pharmacopœia Commission despite the difficulties with which it is obviously faced might sometimes choose official names *that are briefer and more memorable* though perhaps less explanatory (The practitioner can hardly be expected to replace in his mind vitamin B_{12} by the approved name, cyanocobalamin) Then again the increasing number of official booklets on drugs and appliances issued to practitioners points to a need for greater consideration of the doctor's convenience To issue a thick pile of gummed amendment slips for the *National Formulary*, and expect these to be used, is a false economy Up-to date, compact, and well-arranged data on prescribing would do much to prevent waste If proprietary preparations are being prescribed excessively, it is mostly because of the doctor's personal experience and his own and his patient's ingrained habit, and the doctor cannot be expected to forgo his experience and to change his habit unless he is made fully aware of the grounds for such a change Above all, perhaps there is need for continuous instruction of the public which will reduce its pathological appetite for drugs

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[1] See *Lancet*, July 25 1953 p. 191

[2] *Ibid* p 1 7

"Molluscum Pseudocarcinomatosum"

SQUAMOUS carcinoma of the skin was the first tumour to have its histogenesis solidly established—the work of HANNOVER and of THIERSCH has an enduring, if melancholy, memorial in the survival of that unfortunate name, "epithelioma" The chain of discovery of the carcinogens, which runs from POTT through VON VOLKMANN and YAMAGIWA and ICHIKAWA to KENNAWAY, was linked in the first place entirely with squamous carcinoma of the skin The student finds here his best introduction to tumours, for these are the first he learns to recognise with any confidence It is therefore with shock, and some disbelief, that clinicians and pathologists now find that a substantial proportion of lesions which have been termed squamous carcinoma are in fact something quite different

MACCORMAC and SCARFF in 1936[1] described from the Middlesex Hospital ten cases of a lesion they called molluscum sebaceum The lesion was a single nodule, usually on the face, of the size of a small nut, clothed with normal skin except at the summit where there was an adherent scale Microscopically the lesion was a cyst lined by poorly differentiated hyperplastic squamous epithelium, containing keratin, communicating with the surface, and surrounded by an inflammatory exudate Two clinical features were especially noteworthy (1) the lesion grew rapidly to its greatest size in 4–6 weeks, and (2) simple local treatment, even with carbon-dioxide snow alone, was never followed by recurrence This report aroused a good deal of interest, but it is only in the last few years that the condition has been given the attention it deserves

In 1950 ROOK and WHIMSTER[2] published a definitive account of the histology and natural history of the lesion, and MUSSO and GORDON[3] added the vital observation of regression of an untreated lesion, while this year FOURACRES and WHITTICK[4] have clarified and extended the earlier work, and BEARE,[5] with a series of no fewer than 76 cases, has gone far towards establishing the frequency and importance of the disorder The lesion begins with rapid proliferation of a small area of the otherwise normal epidermis, and for a month there is rapid growth of a type indistinguishable from that of a well differentiated squamous carcinoma Local destructive invasion of the superficial dermis,[4] though often doubted, seems to be a definite feature, but the lesion remain delimited, acquiring a characteristic flask soon a large central mass of keratin develop remarks on the almost pathognomonic this mass at biopsy) After 6–8 weeks regression and the highly active squamous epithelium periphery of the lesion settles down to form inactive coating to the central keratin Finally any time up to a year, the plug is discharged remainder of the lesion contracts to form a scar The best treatment is still uncertain remains necessary, for clinically distinction carcinoma is not always possible If either clinician or the pathologist is unfamiliar condit on (and their cooperation is needed for fident diagnosis), complete excision is pro Histological diagnosis depends much on the and size of the whole lesion, and it is not that hitherto many pathologists have failed to nise the lesion when presented, as they usually with a small and perhaps ill-orientated biopsy men In experienced hands a small biopsy suffices for diagnosis Theoretically one might leave the lesion alone, but in practice some will usually be expected, and if well devised ensures more rapid healing and a better scar Nature BEARE claims that shaving the with the surrounding skin and lightly cau base yields adequate material for biopsy and good healing

The true nature of this lesion remains unc Originally it was thought to be of sebaceous but all the recent evidence points to a direct from the epidermis The cycle of rapid growth fol by regression very strongly suggests a virus and the example of molluscum contagiosum show virus infection can produce lesions of broadly shape No positive evidence exists for this contagion has not been proved, the lesion has been transmitted experimentally[5], and no bodies are present Nevertheless, virus infection the most likely cause FOURACRES and W suggest that the lesion may be related to the self-healing squamous carcinoma of FERGUSON and BEARE that it is related to the tumo keratoses of POTH[7]—though this seems less pro "Molluscum sebaceum" is not a very good for it has been used in other senses, and "sebaceous in any case probably misleading Kerat is a colourless term which has not been accepted Possibly "molluscum pseudoc tosum" best epitomises the main features

A good deal of work remains to be done, in a more extensive attempt to transmit the Confirmation of its occurrence in other co would be welcome (It was disappointing to find an account from New Zealand[8] referred only to seen in London) A few cases are known to have seen overseas—for example, in a Spaniard at Gi The lack of reports from other countries is pro due to unawareness of this entity, and there m much to be learnt from its geographical distrib If, as BEARE's figures suggest, as many as one

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1 MacCormac, H Scarff R. W *Brit J Derm* 1936 48 624
2 Rook A Whimster I *Arch belges Derm* 1950 6 137
3 Musso L Gordon H *Proc R Soc. Med* 1950 43 838
4 Fouracres, I A., Whittick, J W *Brit J Cancer*, 1953 7, 58
5 Beare J M. *Brit J Surg* 1953 41, 167
6 Smith J F *Brit J Derm* 1934 46 267 Currie, A. R., J F *J Path Bact* 1952 44 827
7 Poth D O *Arch Derm Syph Chicago* 1939 Fliegelman M T Loveman, A B *Ibid*, 195 66,
8 Purdy M J *N.Z med J* 1953 52, 191

the lesions commonly reported as squamous cinoma of the skin are in fact mollusca, our statistics incidence and prognosis of skin cancer will need to drastically revised

The Banished Bacterium

AT meetings in Rome last month the International mmittee on Bacteriological Nomenclature rejected generic name *Bacterium* and the family name *cteriaceæ* Thus these names are no longer available systematists, but for a time at least *Bacterium* almost certainly continue to appear on report ms

Bacterium has had a long and checkered career It first used in 1828 by EHRENBERG for an organism, *terium triloculare* that cannot now be identified was once applied to spore forming as well as to sporing rods, LEHMANN and NEUMANN used it most gram negative rod shaped bacteria while in latest edition of *Bergey's Manual*[1] it was the eric name for the dump heap of unclassified rod ped bacteria both gram positive and gram ative In this country *Bacterium* was treated with her more respect, medical bacteriologists used it the lactose fermenting coliform organisms which chemists knowing little of bacteriological taxo ny and nomenclature called by the generic names d in *Bergey's Manual—Escherichia* and *Aerobacter* ne, including TOPLEY and WILSON[2] used *Bacterium* gram negative rods that were rather like coliforms , because of significant differences had to be luded from that group—for example *Bacterium tralum* and *Bacterium alcaligenes*

The problems facing the systematist—and these l eventually affect all bacteriologists and even tarians and clinicians—concern the renaming of ny well known species, including *Bacterium coli* l *Bacterium aerogenes* By the rules of bacterial nenclature the oldest name has priority but a mber of requirements have to be satisfied and it is the interpretation of these lesser considerations t doubt and debate may centre Classification st precede naming and the systematists robbed a convenient label for bacteria of uncertain taxo mic position must now do some heart-searching and ide into what genera existing or new these anisms best fit *Bacterium aerogenes* an organism und in water soil fæces and urine exemplifies systematist's difficulties Culturally it closely embles Friedländer's bacillus the cause of severe d often fatal pneumonia and it is also related ologically to Friedländer's bacillus. Some bacterio gists say they cannot distinguish the two, others parate them by origin (above or below the umbili s), a few attempt to distinguish them by differences for example the sliminess of colonies or the ability ferment certain sugars produce gas in fermentation produce the enzyme urease Even those who recog these organisms as separate species generally mit that they fall into the same genus The next oblem is their relation to other coliforms should *cterium coli* be grouped within the same genus? is question is important because on the answer depends the new generic name of *Bacterium coli* Friedländer's bacillus and *Bacterium aerogenes* resemble *Bacterium coli* in being gram negative rod shaped bacteria that ferment lactose but they differ from *Bacterium coli* in such characters as motility encapsulation, urease-production and the end products of glucose fermentation If these differences were always clear cut it would be easy to define two genera but there are so many intergrading forms that generic differentiation is difficult In general British bacteriologists have grouped these species together in the genus *Bacterium* whereas workers in other countries have split them among two or three genera Serologists and biochemists can each separate these coliforms into two large groups and the groups so formed by these workers of different outlook are surprisingly similar A grouping arrived at by two distinct approaches has more to commend it than one achieved from a single angle, and it is likely that, for a time at least this division into two groups will prevail

The problems of nomenclature should be considered in relation to the taxonomic schemes already mentioned For the single group used by British bacteriologists in the past the correct generic name appears to be *Klebsiella*, which has priority over later names such as *Aerobacter Calymmatobacterium* and *Encapsulatus* and by this plan we get the unusual combination *Klebsiella coli* Those who would separate the coli group from the aerogenes Friedländer group will use *Escherichia* and *Klebsiella* as generic names, while any who think that separate genera are needed for *Bacterium aerogenes* and Friedländer's bacillus will have three genera—*Escherichia Aerobacter* and *Klebsiella* How will other coliform bacteria fit into this new naming system? The intermediate types of the water bacteriologists will be known as *Escherichia freundii* and many late lactose-fermenting or non lactose fermenting paracolons (the Ballerup Bethesda and Alkalescens dispar groups) will fall in the genus *Escherichia* Some paracolons are more closely related to *Klebsiella aerogenes* and will be placed in the same genus Other paracolons (such as the Arizona group) are so closely related to the salmonellas that they could conveniently be made a subgroup or species of the genus *Salmonella*

Family names of bacteria are not often used, but one *Enterobacteriaceæ* has become popular as a convenient name for the coliform group of bacteria Plant pathologists object to it because the bacteria pathogenic to plants and related to the coliforms have not been found in the intestinal canal of animals. As a family name it does not accord with the rules and recommendations of the bacteriological code, which says that the stem of a family name should be that of a contained genus—there is no genus *Enterobacterium* By the rules the family name should be *Klebsiaceæ* or possibly *Escherichiaceæ* so perhaps it would be best to accept *Enterobacteriaceæ* as an exception to the rules

The newer names and combinations will seem strange to readers in this country but however much we may regret the passing of the familiar name *Bacterium coli* the use of the generic name *Bacterium* had, in other combinations become an anachronism Surely it is better to make a readjustment now than to continue to use *Bacterium* and be out of step with the rest of the world

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Bergey's Manual of Determinative Bacteriology Edited by R. S Breed F G D Murray and A Parker Hitchins Philadelphia and London 1948

Topley and Wilson's Principles of Bacteriology and Immunity Revised by G S Wilson and A A Miles London 1946.

Annotations

W H O. CONFERENCE ON MEDICAL STATISTICS

APPROPRIATELY enough, Somerset House, where Dr William Farr pioneered the use of vital records, is the venue of this week's W H O international conference on medical statistics No attempt is being made to cover the whole field of medical statistics, the conference is specifically concerned with the activities of the national committees on vital and health statistics established in many countries in recent years The idea of such national committees was first broached at the Paris conference on the 1948 Revision of the International List of Diseases and Causes of Death The aim was twofold—to delegate the intensive study of particular problems of general interest to different individual nations and, by regularly exchanging the special experience of each nation, to raise the standards of vital statistical work in all Stimulated by a recommendation from a later meeting of the World Health Organisation, such national committees were established in 29 different countries, and in 11 some analogous agency of the national health service is carrying out the same function In the United Kingdom, for example, the Registrar General's advisory committee has this responsibility A special unit of the W H O organisation in Geneva coördinates the work of the national committees, whose present interests centre round three main subjects

As we have pointed out before, difficulties in recording the cause of death arise particularly at the extremes of the age scale Special studies of fœtal deaths in relation to the stage of pregnancy, to multiple births, and to birth weight have, therefore, a first claim on national resources of vital statistical research The increasing awareness of the limitations of cancer therapy has given fresh impetus to a search for general factors in cancer ætiology, such as smoke pollution and industrial agents, which may be controlled by appropriate public action But no study of the epidemiology of cancer can be complete without accurate classification of neoplastic disease by site and stage and precise knowledge of the distribution of cancer mortality in relation to time, place, and domestic or occupational environment Sickness which needs hospital care is a heavy national burden For the intelligent administration of a national health service, we must know more about the load, measured in terms of inpatient and outpatient services, imposed by different diseases Where all cases of serious disease, such as the major psychoses, are treated in hospital, the analysis of hospital admission rates among different groups within a community may give epidemiological clues about the causation of mental disorders In other less incapacitating illnesses, grafting hospital data on to the results of special surveys of sickness treated at home may give sound indications of the prevalence of a particular disease and its relation to the several characteristics of the population—demographic, occupational, or domestic—described by the national census

A national committee need not itself undertake the particular study allocated to the country by W H O It serves rather as a catalyst, bringing the needs and interests of the profession to the notice of government statisticians, stimulating fresh work in vital statistics, and encouraging the training of statisticians and doctors in the collation of data from many sources and the interpretation of results Whatever its stage of technical development, these broad needs must be met in any country Whether the formal linking of national committee and international conference is the best way to achieve this remains to be seen, but the present meeting should help to clear the air The presence of Sir Russell Brain, the president of the Royal College of
as honorary president of the conference and head
delegation, supports our belief that modern
cannot afford to ignore the fruits of vital
research It would be idle to expect too much
single conference, the complexities of m
statistical relations cannot be readily solved in
lessons, but the clash of ideas will certainly p
useful fire

COMPRESSION AND BONY UNION

REMODELLING of bone is a dual process of
and osteogenesis, and if the surgeon could dis
actual stimulus to the osteoblast the solution to
problems would be in his hands In his new mono
Charnley reasons that this stimulus is compression
that it is effective only when two cancellous
surfaces are held against each other He be
with compression of cortical bone surfaces this
is ineffective, and he points out that in fractures
is always some death of bone cells in the cortical
adjacent to the fracture site Hitherto the only
mental evidence suggesting that pressure between
surfaces can promote osteogenesis comes from the
of Eggers,[2] done with a bone flap in the skull of
but, as Charnley points out, the forces applied
minute, and there were other factors which might
probably did) affect the rate of union Ch
criticism seems valid, and many will agree with
questioning the value of using slotted plates in
—a method designed to allow the bones to shorten
allowing the muscle tone to maintain pressure
the bone ends as they soften and are absorbed
normal early stages of fracture repair There is
some evidence that pressure between bone ends
harmful,[3] and the enthusiasm for early weight
after fractures is now declining Indeed Watson
condemns this practice He has also expressed
reasons for believing that compression is not
important factor in stimulating union, and C
in the best tradition of the old time pam
(but writing with greater courtesy), devotes a
to disposing of this argument His thesis is based
the work he has done on compression an
particularly in the knee-joint This method was orig
by Key[5] but has been popularised only as the
of Charnley's work It consists in producing two
surfaces by sawing off the joint surfaces of the
end of the femur and upper end of the tibia, trans
the bones with Steinmann's pins, and clamping the
pins together at their ends by means of special
clamps The pressure so generated more or less
the surfaces together, but an external splint from
to ankle is also used This method can also be ad
to other joints Fusion takes place very speedily,
whatever doubts may be felt about the explanation
would deny that the results are much better than
any other method In an uncomplicated case the p
is walking without support, and with bony union be
tibia and femur, eight weeks after operation, six m
(and often far longer) was a more usual period in
past By means of a special trephine, biopsy
mens have been obtained four weeks after op
at which time the pins are removed, a simple p
cylinder is applied, and ordinary walking is allo
and illustrations of some truly superb prepar

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1 Compression Arthrodesis, including Central Dislocation
Principle in Hip Surgery By J CHARNLEY Edin
Livingstone 1953 Pp 264 42s

2 Eggers G W Steindler T O Pomerat, C M *J Bone Jt*
1949 **31A**, 693

3 Friedenberg Z B French G *Surg Gynec. Obstet* 1952 94

4 Watson Jones, R. Fractures and Joint Injuries Edin
1952 vol 1 p 223

5 Key J A *Sth med J* 1932, **25** 909

Prof S L Baker leave no doubt that true union has taken place at that time Baker arks that 'the union of the arthrodesis surfaces nese specimens shows the features of rapid healing ompletely immobilised fracture like that occasionally in an undisturbed impacted fracture, for example a s fracture '

he difficulty is, of course to find proof that it is the pressure rather than maintained intimacy of act alone that has brought about this eminently able result Charnley has designed an experiment, in but a single instance, in which by shaping one bone end into a blunt wedge different areas are ected to different pressures the difference in degree nion in these areas followed his prediction that the ter the pressure the better would be the osteogenesis nother case intimacy of contact was maintained by ling the bone ends together after compression had applied and then immediately removing the nmann pins and therewith of course the spring ment of the compression the usual *dramatically* d bony union failed to result and Charnley suggests this is evidence that intimacy of contact alone is enough It is possible to estimate roughly the sure used from the curvature created in the pins n the clamps are applied, and slow union was found tly in cases where for one reason or another pressure been inadequate

he evidence, so far as it goes, is good but not entirely ifying As Charnley *points out, biopsy material is* cult to come by and indeed the crucial experiment re some form of a pressure gradient is present at surfaces in contact has been done in a single case Charnley of course appreciates that this leaves work open to criticism But whatever one may think he merits of the evidence there is no doubt about excellence of the results With characteristic nuity Charnley has evolved methods by which the ciple can be applied to most joints which need fusion, in the process has evolved the idea of central dis tion as an important, if not vital, principle in surgery

PSYCHE AND SURGERY

HYSICIANS and surgeons in this country were unwilling slow to accept the view that partial gastrectomy is ified in the treatment of selected patients with peptic r; and after adopting resection in preference to tro-enterostomy they have justifiably remained ical of the end results as is shown by many careful ies of the post gastrectomy syndrome and the many ifications of the operation which have been designed educe the incidence of unpleasant sequelæ Even the t open minded, however will be surprised if not ken by the conclusions reached by Browning and seworth[1] after studying sixty patients treated for denal ulcer half by medical measures and half by tial gastrectomy Having followed up these patients at least a year after treatment, they found that the ically treated group revealed a significant decrease ulcer symptoms but that this was offset by a signifi t parallel increase in other psychosomatic and choneurotic symptoms. The medically treated group e not relieved of their ulcer symptoms but did not w the same tendency to develop other complaints over all incapacity was not reduced in either group other words duodenal ulcer is a psychosomatic disease if *effectively treated by surgery* without resolution the associated psychopathogenic conflicts' is likely heir view to be replaced by other no less incapacitating ptoms. Moreover this alarmingly defeatist conclusion is not relieved by any suggestion that the psychiatrist can deal any more successfully with the situation

If this conclusion is not to be accepted it must be refuted with evidence and argument Contrary evidence is not easily adduced because of the absence of similar studies in this country but it must be very unlikely that such seriously incapacitating conditions have been completely overlooked in the many careful reviews carried out here to refer to only one of these Muir[2] a physician reviewing surgically treated patients found that over 90% had some form of post-gastrectomy disturbance (including psychoneurotic symptoms) but concluded that In the great majority of these patients the operation was entirely successful all were agreed that their health was immeasurably improved' For argument perhaps the most obvious and serious criticism of the study by Browning and Houseworth is that their sixty patients were evidently a selected group They admit that the thirty medically treated cases of their control group ' were selected, being patients in whom complete *remission of ulcer symptoms did not occur* *It is difficult* to escape the suspicion that the surgically treated group were also patients who continued to attend hospital because they were not satisfied, if for no other reason than that no less than thirteen of the thirty still had ulcer symptoms For this and other reasons we may reject the conclusions but are reminded that a follow up of patients treated surgically for duodenal ulcer should include a search for other psychosomatic disorders of a conversion type

RECOVERY IN THE LOWER MOTOR NEURONE

WHEN the lower motor neurone is incapacitated, whether by trauma or by infection such as poliomyelitis it is important to find out how rapidly it is recovering and how much recovery may be expected Observation of voluntary contraction of the muscles supplied will give some information, but with a clinically complete lesion this may come too late to be of much value. In *a mixed motor and sensory nerve the course of sensory* recovery from peripheral trauma can sometimes be followed accurately by eliciting Tinel's sign but motor and sensory improvement do not always run pari passu In experienced hands the response of muscle to faradic and galvanic stimulation has proved a valuable source of additional information, and is still widely used It was early noted however, that faradic response was occasionally negative even when voluntary contraction proved that some re-innervation had taken place; and occasionally faradic response could be obtained in a muscle known to be denervated The search for more accurate methods of electro-diagnosis has therefore been pursued and Wynn Parry[3] discusses two such methods—serial strength duration curves, and electromyography

The curve obtained in normal muscle by plotting the voltage required to produce minimal contraction against the duration of the stimulus in milliseconds is characteristic For durations of from 300 to 0 3 milliseconds, the voltage is constant; for durations of from 0 3 to 0·01 milliseconds, it *rises* In denervated muscle also the general shape of the curve is typical. The voltage slowly *rises for* durations of from 300 to 10 milliseconds and for shorter durations than this the curve rises steeply With re innervation the denervated curve shows a kink in its previously smooth outline Further kinks may occur as recovery proceeds and these may combine and widen to give a long plateau until *the curve gradually assumes the normal* pattern Wynn Parry regards these kinks as a reliable and early indication of recovery He has never observed them in cases which did not later show some clinical recovery

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rowning J S Houseworth J H *Psychosom. Med* 1953 15 328

[2] Muir A. *Brit. J Surg* 1949–50 37 165

[3] Wynn Parry C B *Brain*, 1953 76 229

and they precede any signs of this by an average of six weeks Moreover in some cases of nerve injury they appeared, but after a period of development towards the normal showed no further progress, thus suggesting some interference with recovery, and in such cases subsequent operation revealed a neuroma

Serial electromyography also proved of value in prognosis Fibrillation potentials might be observed throughout recovery, and sometimes persisted in small amounts even after full clinical recovery and were therefore of little prognostic value, but discrete low-amplitude potentials of short duration were seen on an average 8 weeks before any clinical contraction These discrete potentials were present even when clinical recovery was finally poor, but where final recovery was good they were followed in a few weeks by polyphasic potentials of longer duration So here also the milestones of good recovery seemed to be clearly indicated

These two methods are to some extent complementary The electromyograph will give more detailed information about that small sample of muscle accessible to the electrode, and if this is luckily placed it may give the earliest indication of recovery The strength-duration curve will give a more coarse assessment of a larger sample it will be less likely to miss the evidence of recovery, though it may record it rather later Both represent an undoubted advance on older methods For accurate interpretation, however, they require technical skill, and, especially in the case of the electromyogram, considerable experience

HÆMANGIOMAS

Angiomas of the skin disfigure but are seldom dangerous It follows that their treatment, undertaken for cosmetic reasons, should be harmless, but this is not always so Among the potentially hazardous treatments which have been recommended are various forms of radiotherapy and injections with sclerosing fluids, including boiling water Cases of aplasia of the breast or of stunted growth of a limb are seen from time to time to remind us that such risks are still taken In some centres, notably on the Continent, frank incredulity is expressed when the visitor remarks that many angiomas regress spontaneously[1–3], and here all angiomas in children are treated, so there is no opportunity to see what happens if they are left alone

The "strawberry" type of lesion is the one most likely to disappear spontaneously It may often be left to do so in areas not subject to friction or to the observation of over-anxious relatives Ulceration does not affect the good prognosis and may in fact accelerate fibrosis Very rapid growth is an indication for treatment, particularly on the face, where a bulky tumour can distort the growth of nearby structures In most cases treatment with carbon-dioxide snow, used with patience and discretion, is quite sufficient In others more complicated methods may be needed, and here the surgeon, the radiotherapist, and the dermatologist should be aware of what each can achieve

The "portwine stain," on the other hand, shows very little spontaneous improvement, except in the mildest examples Sometimes a gratifying amount of blanching may be obtained with Grenz rays without the risk of late radiation sequelæ, but this treatment is not widely available β radiation, in the form of thorium-X paint, has also been used There is a growing awareness that penetrating β-radiation and γ-radiation may occur in this treatment, and the investigations of medical physicists must be carried further before this method can be considered as harmless as was formerly supposed In women the lesions can be successfully concealed with opaque cosmetics for this purpose, but in men the effect may embarrassment if more than small areas are Conway[4] has described the camouflage of flammeus by tattooing pigments into the skin a technique which has been used in the restoration vermilion border of the lip and in the " of facial grafts The treatment is relatively and an area of from 4 to 6 sq in can be treated sitting In seven years 310 patients applied for ment, and of these 85% were selected as likely to from it 159 obtained a result satisfactory to surgeon and themselves—i e, about half those who for an opinion If the lesion is too superficial, pigment is rapidly swept away in the blood, presumably patients with thick, tumid lesions of for example, do not obtain conspicuous benefit W its limitations, however, this seems to be a treatment worthy of further trial

WEANING

From the moment we are pushed willynilly from womb we start to live dangerously, indeed, the passage to the outer world is our first great After that come breathing hazards, feeding and hazards of elimination, all before we have le mothers' arms One very serious risk, which Le Gros Clark[5] thinks we are inclined to und comes at the time of weaning Animals, as they accompanied by their young, through their edible world, manage the tricky business much the young need only watch and copy the pare order to fill their bellies with appropriate and victuals How different is the lot of the human whose internal arrangements seem much worse to deal with contaminating bacteria than those lamb, a calf, or a puppy, and who is conscio anxiously fed by a mother whose ideas derive from social customs and food resources of her communit

In countries where the milk-supply is clean and and mothers are reasonably well educated, the course, are much reduced for clean cow's milk convenient and digestible transitional food for a old enough to be weaned But milch herds are a acquisition in the history of man, and even today of the people in the world have little or no milk mother's milk Suckling and weaning among such peoples has assumed, Mr Le Gros Clark sa magic or ritual significance Only in a few tribes customary to stop suckling the child before the en his first year he is more usually breast fed for an up to four years If maternal milk was his only n ment during that time, he would suffer badly malnutrition, but since other foods are given and even stuffed into him, almost from the start of he commonly suffers from indigestion as well In tribes the mother denies the child the breast fo first few days, or even the first fortnight of life, gives him other provender such as chewed banana This practice at least ensures that only the survive In Rome, Ethiopia, and India butter m the first food given to the child, while the Ba start him off on millet gruel Among the Chag East Africa breast-milk is supplemented, from the s day onwards, with a pap made of milk or butter with unripe bananas and soda (used instead of and from his third month the baby gets a tas everything going, including meat Being used to mixed diet, he hardly notices weaning, except disciplinary action—which, in fact, is the usua made of it

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[1] Lister W A *Lancet* 1938, ii 1429
[2] Bowers R E *Brit med J* 1951 i 121
[3] Walter J *Lancet* 1951 i 475

[4] Conway, H *J Amer med Ass* 1953, 152 666
[5] *Nutrition* Summer 1953 Published by Newman Book 68, Welbeck Street, London, W 1

r Le Gros Clark has many such examples to quote, h well illustrate his point that the human mother e other mammals has no instinctive" way of ing her young; yet her young are more utterly ndent on her than those of any other mammal a the newborn ape nuzzles for the nipple, and res its own safety, when its gymnastic parent moves linging fast to her with hands and feet The depen e of the human infant must he thinks have been atter of gradual adaptations the clinging reflex d not have been safely lost until maternal care had hed a very advanced stage The infant, as we all v, believes in chewing anything he can put into mouth and how he fares on what he chews pre ably depends on the nutrients he can extract from it Le Gros Clark suggests that by the time human its had become as helpless as they are today their lies had become meat-eaters and raw meat can, ays, be chewed with some profit: indeed, Chinese ners still give their children premasticated scraps of The trouble arose when a tribe settled down vated grains, and began to live on a predominantly hy diet. For the staple foods, though just sufficient dults, might then be too poor in proteins, calcium other nutrients to protect the weaned child from us deficiency disease When a child has to learn to on a starchy diet of this kind, prolonged breast ng may give him just the diminishing amount of ein needed to tip the scale of amino-acid sufficiency e question is whether we can raise weaning diets ll parts of the world to an adequate level Mr ros Clark thinks that this might be done by supplying milk, dried skim milk or some milk substitute to les living at such a low economic level that the ren are inevitably malnourished We may also lder some of the cereal and soya mixtures used ssfully in the study[4] recently reported made by Medical Research Council in Germany between 1947 and early 1949 In these mixtures, all the ssary proteins were present, and children aged 11 years did well on them. Even children under a old still throve when about half the milk in their was replaced by such mixtures

MECHANISM OF COLD VASODILATATION

HEN a finger is immersed in ice-cold water intense constriction results. This lasts for about six minutes, is followed by vasodilatation Vasodilatation occurs nervated and in anæsthetised fingers and is therefore ted, at least partly by a humoral mechanism Duff his collaborators[7] have attempted to explore the played by histamine and acetylcholine in this reac

Their technique is difficult and ingenious: a r is inserted in the ice-cold water in a calorimeter the rate of heat loss from the finger gives an indica of the circulation through it. These investigators d that the introduction into the finger of histamine acetylcholine did not influence the vasodilatation ortunately however this provides no definite evidence r for or against these substances being concerned he natural response since it is impossible to be sure the drugs actually reach the blood vessels in uate concentration modification of the vasodilata response can only be observed after preliminary cold constriction so it is impossible to tell whether a introduced into a remote artery has reached the being tested Even when the drug is introduced ugh the skin by electrophoresis its eventual distribu may depend largely on the local circulation and be much reduced when the vessels are constricted cold.

Another experiment, employing a slightly different approach proved more fruitful Atropine was introduced by electrophoresis into one finger, where it was shown to block the vasodilator response of acetylcholine at 29°C When this atropinised finger was inserted in ice cold water its vascular responses differed in no way from those of a control finger This neat experiment suggests that acetylcholine is unlikely to play a part in the vasodilatation induced by cold. In a parallel experiment designed to determine indirectly the part played by histamine it was not found possible as a necessary preliminary to demonstrate blocking of histamine responses at 20°C after electrophoresis of various antihistamines This failure rendered experiments in the cold of no value.

A different finding by this same group of workers originates from the clinical observation that in patients with a high titre of cold agglutinins in their serum the digits may become numb and cyanosed when exposed to cold Careful experiment has shown[8] that this effect is due not to vasospasm but to blockage of small vessels by agglutinated red cells—a change which happily is reversible

VARICELLA ENCEPHALITIS

ENCEPHALITIS is a rarer complication of chickenpox than of measles.[9] Of 6774 cases of chickenpox admitted to the Willard Parker Hospital in the years 1941–50, 18 (0 26%) were complicated by encephalitis[10]—an unusually high figure Few experienced observers in this country can claim to have seen more than one or two cases. Most of the clinical records reported since Underwood's[11] comprehensive review of 120 cases describe single cases It is most valuable therefore to have a new study by Appelbaum and his colleagues[10] of no less than 59 cases 32 of which were observed at the Willard Parker Hospital during the years 1938–52 and 27 in the New York City Health Department during the years 1931–51

The pathology of varicella encephalitis as far as it is known, is broadly similar to that of other postinfectious encephalitides in being predominantly of demyelinating type In each of the 6 reported cases confirmed by histological findings there was damage to the myelin varying from perivascular loss to severe softening of the white matter Inflammatory perivascular infiltration with round cells or fat-containing phagocytes was also present in every case. In addition, degenerative changes in the neurons were observed in 3 of these 6 cases The one necropsy in Appelbaum's series, however showed no loss of myelin, but merely perivascular œdema and slight cuffing This may have been related to the fact that the patient died very soon after the onset of symptoms The most common age for this complication (as in measles) is between 5 and 7 years and of Appelbaum's cases 65% were not more than 11 years of age but the ages ranged from 8 months to 71 years The onset was most commonly between the 3rd and the 8th posteruptive days, although in 1 case it appeared coincidently with the rash and in another case 21 days thereafter The onset was most often dramatic, with headache vomiting fever, and a change in the sensorium sometimes with convulsions and paralysis as well Of the 59 patients in the series, onset was more gradual in 20 with irritability drowsiness and ataxia. The clinical course was very varied almost every sign indicative of central nervous system involvement being encountered; the commonest signs and symptoms in the 59 cases were neck stiffness (29) drowsiness (27) headache vomiting fever (33, 34 39) ataxia (16) convulsions (13) apathy (15) and stupor (11)

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[4] er *Rep. med. Res Coun., Lond.* no. 279 H.M Stationery Office 1952. See *Lancet*, Aug 15 1953 p 331

[7] uff I., Greenfield, A D M Shepherd J T Thompson I D., Whelan, R. F *J Physiol.* 1953 121 46

[8] Marshall R. J Shepherd J T Thompson I. D *Clin Sci.* 1953 12 255

[9] See *Lancet* 1953 i 125 780

[10] Appelbaum E Morton H R., Dolgopol V B *Amer J Med.*, 1953 15 223.

[11] Underwood E. A *Brit. J Child Dis.* 1935 32 83 177 241

The most usual findings in the cerebrospinal fluid were moderate increase in the white cells (only 10 cases showing more than 100 cells per c mm) and slightly increased protein The outstanding differential point in the diagnosis was the concurrence of clinical manifestations of encephalitis with a varicella rash at any stage The prognosis was relatively favourable, the fatality-rate was only 5%, and 80% of the patients were discharged from hospital without any neurological or other detectable abnormalities A follow-up of 33 cases for periods varying from 6 months to 13 years revealed neurological sequelæ in 10, and in 3 of these they first appeared 6 months to 3 years after discharge from hospital On the patient's discharge the prognosis must be somewhat guarded, for occasionally the neurological pattern later changes significantly The treatment in this series was entirely symptomatic, but in view of the work of Kabat et al[12] and of Moyer et al[13] on the suppression of experimental demyelinating encephalomyelitis with cortisone or corticotrophin (A C T H), the administration of these hormones in the early phase of varicella encephalomyelitis should certainly be considered

UTERINE CARCINOMA

Mass statistics play an important part in assessing progress in treatment, and those who have collected data will appreciate the difficulties that Dr J Heyman and his editorial committee have overcome in presenting the results in 83,291 cases of uterine carcinoma from 69 institutions in 15 different countries[14] The improvement in results is shown by the fact that the 5-year over-all apparent recovery rate has increased from 26 3% in a report issued in 1938 to 34·1% in the latest report, and for the latest 5 years covered by this report the rate is 38% Altogether 78,943 cases of carcinoma of the cervix are included, of these, 73,612 were treated 17% were in stage I and had a 5 year recovery rate of 59 9%, 36 2% were in stage II with a recovery rate of 41 1%, 35 9% were in stage III with a recovery-rate of 23 2%, and 10 9% were in stage IV with a recovery rate of 6 7% Cases of carcinoma in situ (stage 0) are not included

Against this background it is interesting to study the excellent results described by Meigs[15] in 100 cases of carcinoma of the cervix personally treated by radical hysterectomy and lymphadenectomy Meigs looks on this series as a pilot experiment, and he deliberately selected stage I and stage-II cases in "good risk, fairly young and not too fat patients" There was no operative mortality, and after 5 years 75% were alive and showed no evidence of carcinoma It is important that of the 100 patients 46 had some preoperative radiation Meigs believes that X ray and radium therapy is still the proper treatment for this disease He calls for closer cooperation between radiologist and gynæcologist and for greater individualisation of radiation therapy, and he deplores routine applications of radiation by the gynæcologically or surgically unskilled radiologist In this country cancer cases are now sometimes referred direct by the practitioner to the radiotherapist and are treated without consultation with the appropriate specialist Such an arrangement will not always result in the patient receiving the most suitable treatment; and the only solution is closer collaboration between radiotherapist and surgeon or gynæcologist

The preliminary results of another experiment in therapy have been set out by Gorton,[16] who since 1948 has treated at Lund 162 cases of cervical carcinoma by extraperitoneal lymphadenectomy after full radiation by the Stockholm method This plan of therapy new, but the material is very carefully presented. 181 patients operated on (including the 162 who went extraperitoneal lymphadenectomy) lymph metastases were found in only 15 5%. This is lower proportion than has usually been found for st and II Gorton claims this as evidence that often destroys carcinoma in regional lymph node concludes that the 5 year recovery rate for cases by irradiation only is about 40%, that surgery has been proved superior to radiotherapy, that an ade dose cannot be delivered to the lymph nodes alo pelvic wall, that the nodes are a common site of rence, and that involvement of the nodes cannot be recognised before treatment It seems a pity that has given such a detailed account when, in more half the cases, only 2 years have elapsed since He rightly claims that with other forms of recurrence rate falls rapidly after 2 years, but it be presumed that this will be so for the treatment chosen

Way and his co workers[17] are treating stage carcinoma of the cervix by radiation followed by ectomy (either radical or simple, depending on rad response) and lymphadenectomy Of 213 cases, showed lymph-node metastases 6–8 weeks after Lymphatic involvement was significantly comm stage II than in stage I, with anaplastic than with entiating tumours, and in patients with tumour in the cervix than in patients whose tumours had after radiation

The difference between Gorton's 15 5% node ment and Way's 45%—both in cases previously —cannot be explained alone by the fact that operated 4 months after radiation and Way 6–8 Considering this difference in the light of Meigs's tion that, among 100 cases, 17 of the 23 with nodes died within 5 years, compared with 8 of with negative nodes, it is clear that very large need to be carefully studied before two treatment can be fairly compared

SCIENTIFIC BASIS OF MEDICINE

In 1950 the British Postgraduate Medical F arranged the first of an annual series of lectures mainly to indicate to young research workers specialists in training the scientific basis of their of other subjects That year the introductory was given by Sir Henry Dale, O M, F.R S, and week, on Oct 8, Sir Henry introduced the fourth Tracing the development of medicine over the past hundred years, he remarked that even at the turn last century there was a progressively dominant tion in medicine, and to a lesser extent in surgery, clinical work was an empirical art or craft—"a priesthood"—and certainly not a science. were not only unscientific but specifically antisc Lacking firm evidence from controlled experimen clinician could take his choice of remedies, and th value of citrus fruit juices in the treatment of and of cod liver oil in the treatment of rickets had repeatedly forgotten and rediscovered Now, it was recognised that the study of the patient follow the scientific method, and firm partne been established between workers in the sciences and clinical investigators In this part chemists were playing a leading part, and Sir cited as an example news that he had lately America of the isolation, identification, and even lation of the oxytocic hormone of the posterior pi a development that he had never pictured when recognised this hormone forty eight years ago

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[12] Kabat E A., Wolf A Bezer A E *Fed Proc* 1951 10, 412
[13] Moyer A. W Jarvis G A, Black J Koprowski H Cox, H R *Proc Soc. exp Biol* N Y 1950 75, 387
[14] Annual Report on the Results of Treatment in Carcinoma of the Uterus Eighth Volume Available from the Editorial Office, Annual Report Radiumhemmet Stockholm 60
[15] J V *Ann Surg* 1953 137 660
G *Acta Radiol Stockh* 1953 suppl 100

[17] Cherry C P, Glucksmann, A Dearing, R, Way, S *J Gynæc Brit Emp* 1953, 60, 308

Points of View

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THE PLACEBO
ITS USE AND ABUSE

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ACCORDING to the *Shorter Oxford Dictionary* a placebo a medicine given more to please than to benefit patient." To me this is a contradiction in terms hing that pleases me does me good Yet it probably *ribes well enough what we mean by the word.* To a placebo may be the correct treatment for a patient needs a material sign that we are trying to help and who from a scientific point of view at any is past our help Like any other treatment, it be misused and the placebo has fallen into the ter disrepute because it can so easily become the ustay of quackery But its intelligent use can be eat help to patients and doctors alike

Uses

For a patient with malignant or degenerative se where no adequate scientific treatment is known diseases as progressive motor neurone disease minated sclerosis, and carcinomatosis often occur *entally active people and terrible depression* and ppiness may be caused by a plain statement to the nt that 'nothing can be done.' I therefore defend use of vitamin E liver or vitamin B_{12} injections and s in these conditions

For psychoneurotic patients who need a material to establish confidence so that they will benefit the real helpful psychotherapy that follows So a patient believes that his doctor has failed ause he only talked to me and words can't help trouble. For these patients I think valerian is est placebo and probably better without the usual ide

For patients in hospital for prolonged investigations. ve given up using placebos myself in this way use I find that patients usually accept an explanation they can understand

Abuses

Giving a placebo instead of taking an adequate ry and making an adequate physical examination is the major crime and the deadliest of medical and has got the poor placebo into disrepute It s most mistakes in diagnosis and treatment—e g., onic for the primary depressive state bromide for hyrotoxic patient, white mixture for the carcinoma mach vitamins for pulmonary tuberculosis

Giving a placebo in the belief that it is a scientific nent This is probably the fault of the wholesale manufacturer as much as anyone I instance the f vitamin B in painful sciatic or other forms of tis the use of certain vegetable extracts in hyper n and the use of testosterone in psychoneurotic tence

Giving a placebo in the belief that no scientific ment exists, when in fact it does Primary depressive may be treated for years with tonics such as anine when the illness might be cut short by oconvulsion therapy

Giving an expensive preparation as a placebo is not uncommon and greatly encouraged by tising

Giving a placebo on demand We all have patients demand tonics cough mixtures something for the s or physiotherapy for minor ailments

6 Continuing to give a placebo for a long time I saw a patient not long ago who had had a urinary infection possibly venereal in origin and ten years later was still on methylene blue

Conclusions

The above list of uses and abuses suggests four general principles for prescribing placebos

The patient must have been properly examined, investigated and listened to
The drug prescribed should be cheap and non toxic
No really effective treatment should be available
The treatment should not be unduly prolonged.

We must beware of prescribing the placebo to please the doctor rather than the patient for a feeling that something has been done may blind us to any change in symptoms and may prevent that constant alertness so necessary to good doctoring Nevertheless there is a not inconsiderable place for the placebo in medicine and if intelligently used I will defend it to the last drop in the bottle

A BOTTLE OF MEDICINE FROM THE DOCTOR

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> Faith in the gods or in the saints cures one faith in little pills another, hypnotic suggestion a third faith in a plain common doctor a fourth (Osler 1901)

> the desire to take medicine is one feature which distinguishes man the animal from his fellow creatures It is really one of the most serious difficulties with which we have to contend (Osler 1894)

> Babes are not born with a desire to take a drug for every symptom—they acquire this desire Who teaches them? You and I do We educate our patients and their friends to believe that every or almost every symptom and disease can be benefited by a drug" (Cabot 1906)

IT has been said that the specialist observes his specimens in the zoo while the general practitioner pursues his quarry through the jungle (Barber 1951) One of the problems that beset the doctor who leaves the zoo for the jungle is the placebo accustomed to using drugs for a well defined pharmacological effect he is puzzled to find inert medicines given as a means of suggestion or because the patients expect them Having recently come to general practice I offer the following observations and reflections with humility in the hope that they may provoke others more able and experienced to throw light on what is now a major national problem My purpose is to consider why placebos are so widely used whether the patient is well served thereby, and what place placebos would have in an ideal practice where there was enough time to work without being hurried Are placebos part of the Art of Medicine, or are they unfortunate necessities?

A placebo is defined as an inert drug given to satisfy the patient. The word 'inert' is vague, and I have included those drugs which have no pharmacological action and those which are commonly given in inappropriate circumstances or inadequate doses mainly for their power of suggestion Among these I would include all tonics most of the vitamin and hormone preparations as currently used and a host of proprietary combinations of old favourites offered in fancy dress and with new names as great advances It could be maintained that many potent drugs such as barbiturates, amphetamine and anti histamine preparations are commonly used so uncritically as to fall into the placebo class.

The scope of the problem is best illustrated by the size of the nation's bill for drugs The estimated cost of drugs prescribed by general practitioners under the National Health Service for 1953–4 is £46$^1/_2$ million, and the number of prescriptions is likely to be over 200 million, that is an average of about 5 prescriptions per person at a cost of a little over £1 In 1952 proprietary drugs represented 26% of the total number of prescriptions and 44 5% of their cost (Macleod 1953)

If the figures collected from 17,301 prescription forms (Dunlop 1952) are a fair sample of the whole, a third of prescriptions in general practice are for tonics, stomachics, and sedative and hypnotics combined, whereas penicillin, sulphonamides, bronchial dilators, iron preparations, cardiac drugs, hormones, liver extracts, and strong analgesics together account for only a fifth

Arguments in Favour of the Placebo

> "Indeed, with the world as it now is nothing could be more calamitous than to rob the people of this kind of sickness, for as things are there appears to be no escape from perplexity and uncongeniality for thousands amongst us other than through the narrow neck of the bottle of medicine To a large extent one of the major social functions of medicine has thus unfortunately become the provision of comfort for the inefficient and of support for those who, because of their own inadequacies, cannot cope with circumstance" (CREW 1953)

Some of the reasons for giving placebos are that the patient expects a bottle of medicine, he has faith in it, and it makes him feel better, the doctor's task is to make the sick whole and if placebos do that they are justified The medicine bottle carries with it a magic charm of suggestion and comfort, and is a token that the doctor has taken upon himself the patient's problems It is harmless, an innocent indulgence which provides the same sort of solace as does the beer or spirit bottle to the patient's more robust friends If the doctor refused to give a placebo the patient would consider that he did not care, was mean, or had given up interest and hope, the patient would go to another doctor who had no scruples about it Many of the general practitioner's patients are unhappy, discontented, and unfulfilled, and comfort is so easily supplied to them in this way

To the busy doctor perhaps the most cogent reason is that it is quicker to give a placebo than to refuse it Those of the profession who feel inclined to criticise the general practitioner's methods should, in fairness, try to imagine how they would cope with an evening surgery at the end of a busy day, when the waiting-room was full and the queue extended down the front garden to the street This is not fanciful, it is the everyday experience of many of the profession and is described in the Collings report (Collings 1950) In such circumstances careful examination, considered diagnosis, and logical treatment or superficial psychotherapy are out of the question, and the only way to work through the queue is to provide each with what he came for, a bottle of medicine

I do not suggest that these conditions of practice are the rule or that they are inevitable, but they are common enough The placebo habit is often due to too much work and too little time, and the only solution lies in smaller lists and better organisation, which we must hope will come with group practice, the Danckwerts award, and ultimately, perhaps, the health centres

The Dangers of the Placebo

1 *The placebo is a form of deceit, initially of the patient, ultimately of the doctor*

We like to think that our patients bring us their symptoms and problems for our consideration, expecting thoughtful and honest advice With the increase in minor psychological illness—"the malaise of maladjustment" (Crew 1953)—and the declining influence of the Church the doctor's value to the community as an impartial and educated adviser has become as important priest's used to be The placebo is a form of deception and a betrayal of trust equivalent to of bottles of ditch-water as water of the River

The faith of patients in the doctor's limits, many are sufficiently critical to recognise which does them no good Perhaps it happens often than we like to think that a doctor gives because he thinks the patient expects it, and the drinks it (or secretly pours it down the drain) be does not want to hurt the doctor's feelings go on for years

> "Placebos have another bad result They confidence of the patient in the physician, because placebo is a lie, and in the long run the lie is found out give a placebo with one meaning, the patient with quite another. We mean him to suppose that the acts directly on his body, not through his mind by of expectant attention If the patient finds out are doing he laughs at it or is rightly angry with have seen both the laughter and the anger—at our Placebo giving is quackery" (CABOT 1906)

Ultimately the doctor deceives himself, loses objective view of therapy, trying out drugs which do some good, without ever being able to find out have It is essential for the doctor to preserve view of therapeutics if he is not to lose himself profusion of new remedies and become a prey drug firms and their new polypharmacy To the there is need for much more postgraduate from the College of General Practitioners, the hospitals, and universities, at present it is largely hands of the drug firms and their travellers

2 *Placebo giving prevents early diagnosis*

The effect of the placebo habit is that di neglected, a short cut is taken from symptoms ment, the underlying reason is lack of time. is that the young man with pulmonary given a tonic until he has a hæmoptysis, and the aged man with a carcinoma of the stomach has of alkali until the growth is self evident and inop Of carcinoma of the lung referred to the th less than a quarter are operable (Brock 1950). figure will be improved only when the general pract confronted with a middle-aged man with a recent onset has the time and facilities to chest and order a chest radiograph instead of bottle of cough mixture

The placebo is a relic of the days when there effective therapy The doctor's duty was to as patient that he was being cared for Now the holds the power of life and death in many dis temporising with bottles of medicine may rob the of his chance of cure

3 *Placebos produce neuroses*

> "But it is a fallacy to suppose that an inactive can do no harm. If prescribed in a perfunctory patient needing explanation and reassurance it may faith in his disease rather than in the remedy, and who gives a placebo in the wrong spirit may patient" (*British Medical Journal* 1952)

Many of the patients in the doctor's surgery because they have come into conflict with their ment or with themselves Although some are tionally and incurably neurotic, many have come for reassurance which would readily set the right road to recovery

A married woman of 46 complained of frequent lower abdominal pain and mild diarrhœa During the there was tenderness and voluntary guarding in fossæ Nothing abnormal was found on rectal exam and the temperature and pulse were normal, she theless, prostrated and kept to her bed In the had a cæsarean section and a perforated appendix removed, it was feared that adhesions might be pres rning I was sent for urgently because she had collapsed with scream of pain and been found prostrate though not onscious. I was able to satisfy myself that there was no anic disease in the abdomen and with a little encourage nt she told me of her worries over her husband, who had rnicious anaemia; the latest haemoglobin estimation was 'o, which to her meant that he was deteriorating rapidly feared that he would have to give up his job teaching in a versity department and then their only daughter would e to leave a fashionable school. She felt caught in a trap lecided which of her family should be sacrificed to the other t was easy to point out that there was no problem there all and that her husband's health was in fact very good accepted this with evident relief and was able to get up d do her work without pain although she was a chronic rier and would need helping through similar crises in the ire.

There is nothing at all unusual about this case and actitioners will be able to recall many similar but it is example of a patient to whom it would be disastrous give a placebo—to be on the safe side—since it would gest to her that the doctor had found something ong So the fear of organic disease is confirmed

Many of our patients behind their trivial and incon uential complaints hide unspeakable fears; fears of cer tuberculosis, blood pressure prolonged suffering okes and sudden death For them we can provide ef only by learning what they are afraid of If he is l that there is nothing wrong the patient decides that doctor does not understand his symptoms if he is en a bottle of medicine his worst suspicions are firmed

Placebos are inadequate therapy

bottle of inert medicine is a poor substitute for ctive symptomatic treatment such as analgesics for ritic pains or barbiturates to provide restful nights, for the careful regulation of the patient's activities , and habits which is necessary in chronic diseases so t he may adjust himself to his limitations and make the t of a crippled life

t may also stand in the way of specialist treatment in pital The increasing complexity of medicine places itional responsibility on the general practitioner since alone can make available to the patient the benefits of specialist departments His patient's welfare depends the doctor being in touch with the recent advances and wing what the hospitals have to offer This is a heavy onsibility and in no way devalues the general titioner's status to that of a sorting clerk. For many ients effective treatment can be provided only by a nber of people working together whether at home or hospital the family doctor has an important place ong them

o nervous patients investigation in hospital is often range and unnerving experience Repeated history ngs, examinations, radiography and venepunctures ncrease the patient's conviction that he is a sick man rring a patient from one department to another tributes to his demoralisation The general practi er can recognise this more clearly than the specialist it is his duty to some of his patients to keep them iome.

Placebos are a waste of time

lthough it may be quicker to give a bottle of medicine a to refuse it in the long run it makes more work n it saves for those who have had one bottle will e again for another and so the surgery will be crowded patients asking for just one more bottle, please

Is There a Place for the Placebo ?

ittle attention has been given to the many general tices where drugs are prescribed sparingly and with rimination Pinsent (1951 1952) in an analysis of l consultations in his practice found that 1458 were administrative The drugs he prescribed at the remaining 6606 consultations could be classified as follows

	%
A. Specific (antibiotics immunisation liver iron insulin, &c.)	10–15
B. Symptomatic treatment with drugs designed to alleviate symptoms as well as to affect the course of the disease	10
C Symptomatic treatment, more suggestive than pharmacological	20–25
D Placebo. Less than	10
E None	40–50

In prescribing these rare placebos Pinsent deliberately used the faith of many older patients that the doctor knows the remedy uniquely applicable to their cases He gave no placebos to patients under the age of 40 instead offering them advice and guidance on how they might help themselves. Medication was replaced by a conscious effort at instruction of the patient, and this change was well accepted by the patients though some whose confidence could not be retained were no doubt lost to the practice Pinsent holds that

> the mother with her first baby requires guidance the young man who fears tuberculosis needs the therapy of a complete examination followed by reassurance the old patient must be taught how to live up to but within, the limits of her failing powers This teaching can only come from the family doctor the general practitioner who is perhaps serving a more useful purpose when he advises than when he prescribes.

This inspiring example of honest therapy makes it clear that, although as a matter of *practical politics* general practice cannot be run without placebos, they need play but a small part in treatment and that time and the fear of losing patients are the chief reasons for *their widespread use*

Conclusion

There is a small place in practice for the placebo as a means of reinforcing a patient's confidence in his recovery when the diagnosis is known and there is no specific treatment Medicine should not become a habit

A patient who asks for a tonic often needs some specific treatment, such as iron for anaemia

Some patients are so unintelligent neurotic or *inadequate as to be incurable and life is made easier for* them by a placebo It has been said that the use of placebos is in inverse ratio to the combined intelligences of patient and doctor (Platt 1947)

It is usually best to humour an elderly patient who has been brought up on the bottle

The doctor who gives a placebo must be certain in his *own mind that it is completely inert, rather than entertain* a half hearted idea that it may do some good

Placebos should not be given if the diagnosis is in doubt particularly if there is any possibility of malignant disease.

Placebos should not be given to worried and distressed patients, who need help in readjusting themselves to their *environment or relief from unfounded fears*

It is a pleasure to thank many friends for advice especially Dr J E Jameson Dr G O Barber Dr A. M. Cooke Dr J A Fisher Dr Doris Odlum and Dr Pinsent and Miss P Browne for secretarial help

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Medical Conferences

CARDIAC PHYSIOLOGY AND SURGERY

A SYMPOSIUM on Recent Advances in Cardiac Physiology and Surgery took place in Minneapolis on Sept 14–16 This was sponsored jointly by the University of Minnesota and the Minnesota Heart Association

Contractile Activity

W F H M **Mommaerts** (Cleveland) discussed contractile activity, admitting that much of the work had been done on striated muscle rather than on cardiac muscle It is presumed, however, that the contractile process is similar in both forms of muscle, though contraction is slower to follow stimulation in cardiac muscle Actin and myosin have been obtained from both Adenosine triphosphate is believed to be used up in cardiac contraction, for if the heart is brought to a sudden standstill by dropping it into liquid air this substance is found, but its concentration is greatly diminished in the beating heart Purkinje tissue has been found to contain a specific acetylcholine esterase which is instrumental in the conduction of stimuli

The account was continued by **Olle Snellman** (Uppsala) In heart muscle a complex of actin, nucleotropomyosin, and protein has been found and termed actotropomyosin It is thought to have phosphatase and deaminase properties and to react with cardiac glucosides

Blood Volume and Heart Volume

Torgny Sjöstrand (Stockholm) had found that capacity of the vascular system, blood volume, and end diastolic heart volume are related to each other The heart volume is related to a person's work capacity, and, at rest and during work, related to the stroke volume and also the total body blood volume The pulse frequency at rest appears to be related to the heart volume and the quantity of hæmoglobin in the body In cardiac failure the blood volume and the heart volume are increased and the cardiac output lowered

Otto H Gauer (Dayton) described the mechanism by which small increments of blood volume cause an increase in pulmonary and systemic venous pressure which stimulates stretch receptors and reflexly causes a water diuresis, restoring the blood volume to normal

Anatomy of Ventricles

R F **Rushmer** (Seattle) described the new anatomy of the cardiac ventricles The left ventricle approximates to a cylinder with a cone on top of it Ejection is mainly the result of reduction in diameter of the cylinder Such architecture is well suited for ejection of blood against a high resistance In contrast the right ventricle is bounded by the convex interventricular septum and a free wall which is concave This shape has a much greater surface area per unit volume than the left ventricle and is adapted to ejecting large volumes against low resistance When the right ventricle hypertrophies against pressure it comes more to resemble the left Observations of ventricular diameter, using intraventricular gauges in unanæsthetised dogs, have shown that neither ventricle empties completely, so that increased stroke volume may be achieved either by more complete ejection or by greater diastolic filling When the animal is startled, an increase in systolic and diastolic heart size is seen within the space of one beat, the manner in which this occurs is not known, but the effect is that tension can be maintained with a minimal shortening of the myocardial fibres Atrial systole does not result in a material volume increase of the ventricle

Oxygen Transport

R W **Stow** (Columbus) considered the systematic errors which may occur when the Fick principle is applied to oxygen transport The measurement of oxygen consumption may not be reliable, and if the rate of flow and the oxygen content of blood at the sampling sites vary in a cyclic manner certain discrepancies may occur The importance of these factors cannot yet be determined A **Cournand** (New York) reported that Dr **Gregg** (Washington) had found that the Fick method does agree with a direct method (Rotameter), but this may not be so when low concentrations of oxygen bed

Flow and Pressure in Arterial System

Discussing flow and pressure in the arterial WETTERER (Munich) considered two physical systems of the air chamber *Windkessel*, and those of the elastic the arteries He suggested that determination of di may be based on volume pressure relationships of parts of the arterial system or indirectly on of the pulse wave velocity As so measured, the disten of the arterial system appeared to be more closely body-weight than to age and sex

E **Wood** (Rochester, Minn) emphasised the desirabi determining the characteristics of any measuring and the impossibility of eliminating artefacts when through a cardiac catheter

Cardiac Output

C W **Sheppard** (Oak Ridge) considered the dye technique of estimation of cardiac output. Even in of a dye being simply injected into a straight tube which water is flowing steadily, the mixing curve differ what would be expected, in particular, the dye appea than the theoretical appearance time To take into the movements of dye within the fluid as it passes the web of the capillaries the statistical approach "random walk" is used Instead of time the fraction circulatory bed displaced is chosen as the variable, so that the curves come to depend on a ing constant" This theoretical approach can partia the form of the dye curve obtained

Stroke Volume and Pulse Contour

The relationship between stroke volume and pulse was discussed by J W **Remington** (Augusta) He f the net volume increase of the arterial bed during sy be equated with the time pressure area under the contour By this means the volume increase can be mined under 25% in man and within 15% in dogs area under the pulse contour is further corrected for th increase due to the pulse wave, the stroke volume determined to within ±15% of that found by appl the Fick method On occasions, however, the two volumes become markedly divergent It was also simple formula employing pulse pressure and (Erlanger and Hooker) gave a measure of cardiac sufficiently accurate for clinical purposes

Diagnosis of Congenital Heart-disease

L **Dexter** (Boston) dealt with methods of d congenital heart disease The cardiac catheter is useful in the diagnosis of a left to right shunt, though of the exact site of the shunt may be difficult. If the fails to give clear evidence of a shunt, it is unlikely shunt is of clinical significance Catheterisation demo a stenosis by showing a pressure drop over the const and the finding of equal pressures in the two ventricles a free communication between them The diagnosis patient with complicated congenital heart-disease be made on the findings at catheterisation alone but that all available data should be put together

H J C **Swan** (Rochester, Minn) dealt with the dye dilution curves in the diagnosis of congenital disease He demonstrated how the time-concen relationships of an indicator rapidly injected into the lation are affected by the vascular pathway traversed there is a right to left shunt the interval between the and the first arrival of the indicator at the sampling shortened, there is also a double-hump pattern due dye which has not traversed the shunt With a left shunt the appearance time is normal, but the slope declining curve is prolonged because of the recirc through the pulmonary circuit It is possible to estima approximate size of the shunt from these curves, injections into different cardiac chambers it is poss localise the shunt To take full advantage of the it is necessary that the observer should evaluate his at the time of catheterisation

E V **Newman** (Nashville) emphasised the diffi calibrating the concentration of the blue dye T 1824 a background of cyanosed blood The shape of centration curve obtained may depend on the rate at d is caused to flow through the sampling tubes. When oncentration of the dye is rapidly changing it is difficult ot representative samples.

T Dotter (Portland) showed how angiography had d in the diagnosis of cases of congenital heart-disease

Surgery of Mitral Valve Disease

E Harken (Boston) dealt with the surgery of mitral disease In the very seriously ill operative mortality is very high (28%) but in the less severely ill mortality fallen from 14 to 3% It is likely that the mortality be still further reduced if emboli can be prevented A ier improvement has been to avert disturbances of water sodium metabolism during the postoperative period preoperative recognition and the surgical treatment of al insufficiency remain difficult Harken is attempting to ce mitral insufficiency by fixing a plastic bottle under the al valve 24 such operations have been done on severely tients. There were 7 operative deaths. 11 patients have ved for two years after operation, and 5 were greatly oved by the operation There is no evidence that the closes up after valvotomy though the myocardium may In discussion C W Borden stated that a stenosis which l be widened had been found in 4 patients with massive ation of the left atrium.

C. Bigelow (Toronto) showed how surgical treatment of al stenosis had had a favourable effect on the course of disease L Dexter (Boston) is impressed with the er of continuing rheumatic activity and recommends aylactic penicillin routinely after operation.

Approach to Aortic Valve

P Glover (Philadelphia) showed how the aortic valve much more difficult to approach than the other heart s. To go through the left ventricle is not easy and the ion leaves the myocardium in a weakened condition The oach to the valve through the aorta has not been success He favours the use of an expansible dilator introduced the left ventricle If the patient can be operated on e florid calcification occurs, so much the better During years 23 patients have been operated on ; 3 showed lent results, and 9 were improved (though 3 of these quently died) ; 2 were unchanged and 8 died

A. Hufnagel (Washington D C.) described his method e introduction of a plastic no return valve into the aorta tients with aortic insufficiency 20 patients have been ted on, and 15 are living and improved ; in the last 10 there has been 1 death from myocardial failure He considered the possibility of treating aortic stenosis by rting it into a regurgitation and treating that.

Heart lung Apparatus and Hypothermia

H. Gibbon (Philadelphia) described the application of a anical heart lung apparatus to cardiac surgery The for such an apparatus arises because cardiac defects ot always be dealt with satisfactorily unless the lesion e seen and there is adequate time for its repair Lowering ody temperature permits an increase in the time over h the circulation may be stopped but the time available ll short and the procedure is not without danger For een years Gibbon has been developing a mechanical lung apparatus. On May 6 1953 the objective of these of work was attained when the apparatus took over the ation for twenty-six minutes during the closure of an septal defect in an 18 year-old girl

D Dodrill (Detroit) described how the blood-stream be diverted from either side of the heart. He had that one lobe of the lung could suffice for respiration, at blood from the pulmonary vein could be pumped into ubclavian artery on the same side. With this diversion e circulation mild hypothermia might be used In the ary of the discussion Dr Gibbon said that it might inadvisable to cool adults below 32°C.

G Bigelow (Toronto) had found that with cooling of imal the oxygen requirement steadily declines until at it is approximately 15% of normal Young animals tand cooling better than old ; there are marked species nces, and investigations of hibernating animals are being d out At 21 C a distinct change may occur and circu failure may suddenly develop Anti histamine drugs aid the fall in temperature and the compound Win 2 173 may prevent the severe bradycardia. In Toronto cooling to 30°C has been successfully used to aid a patient with mitral stenosis and congestive failure through a valvotomy Rewarming is done by immersion in warm water or by means of a radio frequency inductive machine

F J Lewis (Minneapolis) preferred cooling the animal by diverting a portion of the blood-stream through a cooling coil 6 patients had been subjected to hypothermia during the repair of an atrial septal defect Of these 2 had not survived the operation, and 1 had died suddenly on the third day Air embolism was prevented by continuous aspiration of the left ventricle and defibrillation satisfactorily dealt with by electric shock and cardiac massage Hypothermia had also been used in the excision of a tumour of the *liver R J Bing thought it possible that when the* heart was cooled anoxia of the myocardium might occur because the reduction in coronary flow might exceed the reduction in oxygen metabolism.

Atrial Septal Defects

C. Crafoord (Stockholm) described the techniques of selective angiography of the heart and great vessels He showed how the left atrium could be punctured directly if a needle was pushed in from above the 9th rib on the left side posteriorly Occlusion of a pulmonary artery by means of a cardiac catheter bearing an inflatable balloon had been used to test whether a lung could be resected when the opposite lung was also diseased Lastly he described a Danish operation for closure of an atrial septal defect in which the right and left atria are separated along a line of cleavage between them as far as the rim of the defect which is then closed by sutures.

H Swan (Denver) discussed the various methods for the closure of an atrial septal defect. In his laboratory a closed method has been developed in animal experiments but for patients he favours the use of a visual method in an open heart during hypothermia When the atrium is stretched by the tapes occluding the superior and inferior venae cavae the walls of the defect come together and surgery is facilitated Air embolism is avoided by tourniquets round the lung roots and flooding the chest with saline before closing the heart In one operation the circulation was stopped and the defect closed in 7 minutes 50 seconds

Pulmonary Stenosis

W J Potts (Chicago) considered the surgical treatment of pulmonary stenosis. When a ventricular septal defect is associated with the stenosis the malformation may be treated either by a shunt operation or by a direct attack on the stenosis He favours the shunt operation because the mortality is lower and the results equally good An aorta/pulmonary artery anastomosis is done if the aortic arch is on the left otherwise a subclavian pulmonary anastomosis is done In children below three years of age the operation is done as an emergency operation ; the mortality is high (15%) but in 192 older patients the mortality was only 3 1% Pulmonary stenosis without ventricular septal defect is treated by incision and dilatation of the pulmonary valve

Physiology of Congestive Failure

W F Hamilton (Augusta) in the George E. Fahr lecture showed that a simple theory that disturbance of the balance between capillary filtration pressure and plasma oncotic pressure caused cardiac oedema was inadequate Salt balance renal hæmodynamics and hormonal changes must certainly be considered He had studied the problem in dogs whose left atrium had been narrowed by means of a ligature If the ligature is tight enough these dogs develop distinct ascites, which disappears when the ligature is slackened No leg oedema occurs and this is thought to be due to the development of collateral circulation The pressure in the abdominal veins is not high and apart from an increase in paralobular veins, the liver appears normal Plasma protein and sodium are both reduced and the renal creatinine and P.A.H. clearances are both low The condition, which is ameliorated by giving carboresin, is thought to be comparable to congestive cardiac failure Investigations of the effect of the adrenals and the pituitary on the condition are still proceeding

Special Articles

SURVEY BY THE MINISTER

At the annual meeting of the Executive Councils' Association (England), at Torquay, on Oct 7, Mr Iain Macleod, the Minister of Health, referred to the constitution of executive councils, the continuing shortage of dentists, the heavy cost of prescriptions for drugs, and the improving coöperation between general practitioners and local health authorities

CONSTITUTION OF EXECUTIVE COUNCILS

Mr Macleod said that it had been suggested that the constitution of executive councils should be changed, because the professional members outweighed the lay members In fact there were 13 lay members to 12 professional members, and the real trouble was that the lay members did not always attend as regularly as the professional members In this respect the members appointed by local health authorities appeared to be by far the worst Authorities could appoint outside people, and this should be more often considered

DENTISTS AND ANCILLARY WORKERS

Before the National Health Service began, said Mr Macleod, the Teviot Committee estimated that 20,000 dentists would be required to provide a public dental service The National Health Service had shown that on average each dentist could treat approximately 800 patients a year Taking the present population and making due allowances for all those already toothless, and for the children and expectant mothers who ought to be seen more often than once a year, one arrived at a figure which might well be between 40,000 and 50,000, and this was likely to be far more than the country could afford in terms of both money and man-power

There was not an unlimited number of people of the right calibre to become dentists, and present indications were that it would be impossible materially to increase the present annual intake of about 600 dental students, which was barely sufficient to maintain the profession at its present level of about 10,000 dentists in general practice

> " It is surely but common sense to see whether some of the more simple work now done by dentists with four or five years' training cannot be done by rather less highly qualified workers working under a dentist's supervision But as the law now stands we are hampered here, even in making experiments, by the fact that, with the minor exception of oral hygienists (who scale and polish teeth) working under supervision in clinics and hospitals, it is illegal for anyone other than a dentist or a doctor to do any kind of work in the mouth "

The Government had announced its intention to reintroduce the Dentists' Bill as soon as the Parliamentary timetable permitted This Bill, which was before Parliament last year, included provision to enable experiments, controlled by the dental profession themselves, to be carried out in the training and use of ancillary dental workers who would extract and fill teeth under the supervision of dentists

If as a result of experiments carried out under the Bill, which would necessarily take some years, it were found advisable to introduce ancillary dental workers under careful control, this should enhance the importance and status of the dentist It would give dentists the opportunity of becoming heads of departments in clinics and hospitals where the more simple work might be carried out by ancillary workers under their supervision, with their own much greater skill and experience for the more difficult and interesting cases

" Then we might at least see the end of a many dentists spend more than 50% of their work requiring only a fraction of the skill and they have acquired in their training "

THE DRUG BILL

Mr Macleod declared that the cost of —£46,300,000 a year—was prejudicing many other urgent developments in the National Health He proposed to explain the facts to doctors and their help, and to supply them with all the he could to help them to help him in keeping cost of the drug bill He had just sent to all practitioners a list showing the prices of all remedies and of their standard equivalents, and suggestion of the British Medical Association the medical officer of the Ministry was appealing appropriate medical authorities to see whether information on the cost of prescribing could not in the course of medical education Executive might be able to help by taking advantage of opportunities to explain to the public the using the health service sensibly and to point patients must not expect doctors to prescribe for whatever they thought they ought to have particular, household remedies for self medication things patients were expected to buy for th

GROWING COOPERATION

Special reports from local health authorities shown growing coöperation between general pra and these authorities

At *York* three general practitioners asked for to be allocated to attend antenatal clinics run for patients in their own surgeries, and this has been by the local health authority

At *Wolverhampton* a coördinated scheme of based on a somewhat similar procedure has been between the local health authority and the local practitioners which should result in the best use being of the facilities provided by the local authority's clinics and of the services of the doctors

At *Gloucester* a special nursing service has been to relieve general practitioners of night visiting for the of, for example, giving subcutaneous injections

In *Staffordshire* a scheme is now in operation in of the county by which the general practitioner chronic sick case, which he considers cannot be home under prevailing circumstances, to the area officer, who then tries to make suitable arrang the patient to remain at home through the provision of nurses and home helps This has resulted in many being nursed at home who would otherwise be rem hospital

The need for a social worker in the general prac team had already been voiced When one looked field covered by the local authorities in their as local health authorities and " welfare " au one found a wealth of resources waiting to be including visitors to the blind and visitors physically handicapped in one group, the duly au officers and mental health workers in another, and third a wide range of arrangements for the often by voluntary workers, of old people, largely by the Old People's Welfare Co was here that the right type of social worker perhaps be found The first step was a proper between this great band of welfare workers general practitioner—a process which in a few had already started but which needed to be much further The Minister said he would like the social worker as a member of the general prac clinical team—particularly valuable in helping care for the unmarried mother, handicapped the old people—and to develop the closer link up he social and welfare functions of the local authority ch ought to be regarded as complementary parts of service to the public

MEDICAL PROTECTION SOCIETY

DDRESSING the annual meeting on Oct 7, Sir ERNEST K CARLING, the president said that last year the ety had received more than 2000 requests for advice revised rules for coroners, which the society's esentatives had helped to formulate, were now in ation, and he believed they were proving successful giving evidence at inquests pathologists should, he ight, take care not to express opinions on clinical ters, as they had recently been doing in one or two ts. The pathologist had the advantage of being wise r the event but was exempt from the responsibility eciding what treatment the patient should have while alive. Coroners therefore should not attach impor e to the clinical opinions of pathologists who spoke side their proper province. As regards complaints patients negotiations were in progress with the istry of Health concerning the procedure under h hospital authorities were enjoined to indemnify nselves by putting the responsibility on members of r staff (So far had this procedure been carried in one case the hospital authority, in repudiating ility on its own behalf presented the plaintiff's itors with a series of points in which, as it alleged, the ndant doctor had been negligent—and of course the itor for the patient adopted these allegations in an nded statement of claim) Sir Ernest had reason to eve that in the very near future a modus vivendi would reached enabling hospital authorities and hospital s to collaborate fully over claims made against them unsatisfactory relation between doctors and hospital orities was bound to react in some cases to the iment of the patient.

he provisionally registered doctor was now entitled, all other registered practitioners, to all the services he society To practitioners not yet provisionally stered, however no indemnity could be offered gh the society's advice was at their disposal This ation was really rather serious because many hos ls had no house-surgeons or house-physicians at all ne region there was a shortage of 100 housemen in another a shortage of 60 Lacking housemen hospitals employed students and the responsibility with those who employed them The newly qualified could not, in some cases take one of these vacant s because they were not recognised as suitable for training of men seeking provisional registration

he President regretfully noted the continuing ten y to increase the amounts of damages awarded by courts. If this continued at the same pace the iety's annual subscription—so reluctantly raised— ht have to go up further

r W M MOLLISON, the treasurer, said that, at over ,000, costs and damages paid on behalf of members year amounted to £5000 more than in 1951 but raised subscription enabled the society to show a urable balance of about £8400 on the year's working er paying a tribute to the work of Mr S Rayner society's financial secretary Mr Mollison drew ntion to the cards sent out with the annual report tled Statutory Notifications to Public Authorities Reporting Deaths to Coroners. These summarised facts admirably and their usefulness to final year dents had already been recognised by medical schools ch had ordered supplies.

he President and Treasurer were re-elected for a her year and Dr Alistair French received warm nks for his services as secretary to which office he was re-elected Appreciation was also expressed of work of Miss Remington as assistant secretary and Messrs le Brasseur and Oakley the solicitors, whose esentative Mr W G Hawkins addressed the meeting vote of thanks to the President was proposed by F Harwood Stevenson chairman of council.

The annual report, issued by the M.P.S. from Victory House Leicester Square London W C.2 shows that the society has continued to make steady progress and at the end of last year had a membership of 27 960 With resources exceeding £156 000 and reinsurances with Lloyd's under writers its financial position is strong and the council are satisfied that it can meet any demands which members may make Members are encouraged to consult the secretary on any medico-legal or ethical problem affecting their professional work, character or interests" and, as usual they are asked to bring their difficulties to the society *at the earliest possible stage*

GRADING OF S.H M O s

THE following statement concerning review of senior hospital medical officer gradings has been issued by the British Medical Association:

At the annual representative meeting in July 1952 considerable disquiet was expressed regarding alleged injustices following the review of S.H.M.O.s which had taken place some months earlier and a plea was put forward that there should be a right of appeal to some central body against decisions of the review committees. As a right of appeal had previously been refused by the Government the Central Consultants and Specialists Committee did not feel that any useful purpose would be served by pursuing the matter but the committee gave an undertaking that the committee would raise individual cases of apparent injustice with the Ministry

The committee subsequently examined the claims of those S.H.M O.s who had expressed dissatisfaction with their grading and sought advice from independent sources. As a result the committee was satisfied that there was prima facie evidence for suggesting that in certain cases injustice had been done and these cases were brought to the notice of the Ministry The Ministry replied that the status of all the practitioners originally graded as S.H.M O.s had been thoroughly reviewed on more than one occasion and that it was clearly under stood that the review at the end of 1951—the machinery for which had been agreed with the Joint Committee—would be the final approach to the problem The Ministry stated that it was always ready to satisfy itself that in any particular case the proper arrangements had been made for the review of grading and it had ascertained that in each case to which its attention had been directed the fullest consideration had been given by a committee which was expert, locally informed, and constituted in the agreed manner The Ministry thought that no central appeal committee could enjoy all these advantages and it saw no reason therefore for reopening the question.

The matter was thereupon taken up by the Joint Committee which informed the Ministry that while it did not doubt that the review committees had been properly constituted it did not feel that the possibility of error should be ruled out. The Joint Committee stated that in its view the cases to which the Central Consultants and Specialists Committee had drawn attention provided evidence of mistakes in grading sufficient to justify further investigation and it urged that they should be examined again

The following reply has now been received from the chief medical officer of the Ministry

> I promised to consider further your suggestion of an informal meeting with documents to discuss the grading of certain Senior Hospital Medical Officers. I have now done so in the light of what was said at that meeting and on previous occasions when we have discussed these matters of grading
>
> I must say after the fullest consideration that we are unable to accept the suggestion of a further review of these gradings. The review in 1951 was entrusted with the agreement of both sides to specially constituted professional committees and was accepted by both sides as final I cannot see how we could justify questioning the decisions of these committees which were made on that understanding and have now been put into practice It seems to me it would greatly increase the difficulty of ever making any settled arrangements if matters so definitely and finally decided could be reopened.

In England Now

A Running Commentary by Peripatetic Correspondents

We have a medical friend who has several times credibly informed us that he had never had his opinion publicly polled, and when we met him the other day he was at pains to tell us that this stigma had now been removed The great moment arrived as he was sitting peaceably in the Union Station in mile-high Denver, waiting for the Rocky Mountain Rocket to bear him away to Chicago He tells us he was approached by a young lady bearing a bulging despatch case, who sat down beside him "I'm not trying to sell anything" said the young lady hastily, with a trace of discomposure, "I'm a public-opinion poll, and would you care to answer some questions?" Our friend was at once in the picture, and leaned forward eagerly, his tongue trembling with the urgency of his opinions on mile-high Denver, Senator McCarthy, the British National Health Service, and the decadence of the Broadway theatre

The young lady opened her bag and with difficulty extricated a large pile of dilapidated trade periodicals with titles like *Aluminum* and the *Precision Blockmaker's Weekly* "There," she said, "have you read any of these in the last week?" Our friend admitted his oversight, but excused it by his foreign origin "My!" exclaimed the young lady, "to think I'm listening to the tongue Shakespeare spoke! It always gives me a kinda cold feeling right here!" She indicated the back of a shapely neck, and gazed in admiration at our friend, who had not appreciated his linguistic capabilities in this light before It was with difficulty that the young lady remembered the rest of her mission, and produced for our friend's inspection a number of packs of cigarettes of all degrees of magnitude from Bantam to King size Our friend was forced to admit that as a non-smoker he could offer no constructive opinion on them, and the poll was over, leaving behind it on both sides a sense of mild frustration

Determined that the young lady should have his opinion on some subject, our friend hazarded his belief that taking public-opinion polls in the Union Station in mile-high Denver must be an arduous occupation His interlocutor agreed "But you should see me next week," she said, "I'm doing girdles and bras"

To his lasting regret, our friend couldn't make it

* * *

I once went to a lot of trouble studying foreign languages and now I wish I hadn't The aged chambermaid of my small hotel has just given me a twenty-minute recital of her symptoms She has told me about her rheumatism, her mother's rheumatism ("This as a doctor you will find interesting"), the state of her digestion, and the effect of various articles of diet thereon She told me how she found herself a little weak, and she had only seventy-five years She thought she might have a *Krebs*, but her doctor thought not What did I think the pain in her back could be due to? Then she thought it perhaps might be the *Verstopfung* under which she always suffered bad Sometimes to eight days I took avoiding action by assuring her that of the *Todesscheinen* I had written, not one single had been on account of *Verstopfung* She seemed relieved, but I shall get more later

Before the war this wretched half-knowledge of tongues was always getting me involved with foreign officials, usually for bringing the wrong money into their countries sometimes for taking it out They always spoke their own language better than I did and argued me off my feet Often have I cursed my stupidity in not putting on the blank exasperating expression of the honest monoglot Englishman who wins every time without opening his mouth Another way out of course would be to speak the language as well as the natives, but if any true-born Englishman can do that he has no business to After such humiliations I find myself taking comfort in the opinions of my great-aunt long deceased She held that there were two sorts of people in the world, ourselves and foreigners By some strange error of Providence many of the most famous cathedrals, museums, and picture galleries were situated abroad, and one could not visit them without meeting though one would naturally meet as few of th possible They were strange people who seldom English properly Their way of life was insanitary morals unmentionable, and their habits distasteful. were always having wars with one another, and we English out of goodness of heart sometimes allowed ourselves to be drawn in

And then of course they could not make tea.

* * *

It is a source of continual humiliation to me I cannot learn the dosage of penicillin Only they came and told me that one of the monkey sick and asked me to write out a prescription "Penicillin," they said, "that's what it needs" I they had said quinine, now, or morphine, or ma I would have had a firm grip on the situation

The fact is, I am a pre-penicillin man. When pharmacology it was at the feet of a muscular and preceptor who insisted that morphine and mag were the only two drugs a doctor needed But e those happy days my security was being undermi the manufacture of 'Prontosil' or some such stuff (I never did find out the dose of that either)

I am a dead loss to the drug houses. Every m a shiny surrealist picture arrives advising me passing of yet another pharmaceutical mil *safe* brand of succinylcholinesterase an I no longer even turn pale At the mention of barbitone something stirs dimly in my subcon but it goes again directly I can see that my despise me When they decide they need a to look at me contemptuously and say "I suppose good asking *you*, is it?" before they dash along chemist They are quite right, it isn't

Come to that, I am a pre-electrolyte man too wasn't all this nasty sodium about when I was But then again, when I studied medicine people own blood-groups and stuck to them, and you smoke all you wanted without the statisticians at you

All this, of course, is sour grapes. I envy heartedly those gifted souls who can dash off an "rep mist" with a flick of the wrist in the full co that the chemist won't ring them up and have a little chat with them Chemists always ring me about the monkeys I can picture them sniggering to themselves behind their green and red bottles they dial my number "About that pres doctor," they say apologetically, "it's for three l lethal dose I thought perhaps I'd better check you"

It is possibly just as well that my therapeutic is now confined to monkeys But I wish they always need penicillin

* * *

THE NEUROLOGIST'S LAMENT

Long pants!
Do they *all* have to wear them?
Long pants!
Don't they know I can't bear them?
Gastrocnemii hidden—no A J.s I see,
I can't get within striking range of the knee,
And how *can* I, I ask you, test pain at L3?
Long pants!

Long pants!
Roll them up a bit, do Sir!
Long Pants!
Stop! Your leg's turning blue, Sir!
My physical findings could not be much vaguer—
"Vibration sense doubtful six inches of Jaeger"
And how can I tell if the chap's got lumbago!
Long pants!

Long pants!
What if Dad always wore them?
Long pants!
Can't they see I abhor them?
Corsets I cope with, and bras I can master,
I've examined abdomens through holes in a plaster
But if anything courts diagnostic disaster,
It's—LONG PANTS!

Letters to the Editor

ORTISONE IN RHEUMATOID ARTHRITIS

ı,—For some time we have felt that patients and public are being given on the whole an unduly urging view of the use of cortisone and cortico in (A C T H) in rheumatoid arthritis. The publicity by the *Times* of Oct 2 to some rather pessimistic ments *in the October issue of the Practitioner* leads offer our own more hopeful opinions

the *Practitioner* Dr William Tegner points out that sone can have a profound and gratifying effect in ressing the activity of rheumatoid arthritis but he says that after early hope and optimism, dis intment inevitably follows.' From more than three of experience during which time we have returned previously incapacitated patients to an active life latively small doses we regard this second statement o strong No doubt prolonged treatment may with it a host of difficult and even dangerous effects, such as addiction fluid retention cardiac rrassment and mental change' but the art of ine lies largely in obtaining the effects desired t avoiding unwanted sequelæ and cortisone is far being the only drug which is capable of causing Admittedly it is more difficult to use properly was at first hoped, and this has discouraged many ians, on both sides of the Atlantic But we have l it possible to achieve success in a majority of if enough time and trouble is taken.

his *Practitioner* review of advances in medicine D M Dunlop *points out that* when *cortisone is* quiescent infections such as tuberculosis may be ed hypertension made worse or a rebound of rthritis occur on stopping treatment Certainly all possibilities should be well known to anyone using one or A C.T H Such infections must be excluded *e cortisone* or A C T.H treatment is considered for are absolute contra-indications to its use. Also ment never should be stopped abruptly but tailed very gradually

ofessor Dunlop goes on to say that in rheumatoid itis "there is some evidence that in the long run ultimate state of patients controlled by cortisone is etter than those controlled by adequate doses of in' This amounts to saying that both drugs ess but do not cure the disease We would agree in those cases where such suppression can be iately produced by aspirin this should always be lrug of choice it is only in cases where simpler fail that cortisone is indicated His advice that ore using cortisone it is necessary to balance carefully the beneficial effects against the which its use involves is surely applicable to the f any powerful therapeutic substance On the other Dr Tegner's statement that the early beneficial may need progressively larger doses for its tenance' is contrary to our own observations.

believe that the present status of cortisone and H in the treatment of rheumatoid arthritis would iore accurately stated as follows These drugs itute the only quick acting therapeutic weapons ssess with which we can in many cases completely ress the signs and symptoms of this disease They ot applicable to all cases and indeed candidates ich treatment must be carefully selected for there nany known contra indications These substances ery far from foolproof and considerable experience eir use is required if good results are to be main d Patients on such treatment must be constantly ved for their therapeutic needs and responses may rapidly We fully agree with Dr Tegner that such ment should be associated together with the other basic forms of treatment designed to prevent deformity and never as the sole therapeutic method

W S C COPEMAN
O SAVAGE

Rheumatism Department,
West London Hospital.

SMOKE AND SULPHUR

SIR —Being concerned with the efficient domestic use of solid fuel, I was greatly interested in your leading article last week and should like to make some observations on a matter of fundamental importance to the problem of atmospheric pollution

It is in many ways unfortunate that the National Smoke Abatement Society—whose work merits all possible support—should have the title that it has and that campaigns against atmospheric pollution and those against smoke should be confused in the public mind. If smoke abatement campaigns and smokeless zones are designed to reduce the amount of dirt in the atmosphere, they are well conceived It must however not be assumed that they are at the same time reducing the toxic elements derived from the combustion of coal or other fuels

It is clearly appreciated by medical opinion that one of the most probable causes of increased mortality from fog is the high concentration of sulphur dioxide and sulphuric acid in a foggy atmosphere. Indeed support *for this view is given by the paper on the effects of inhalation* of sulphur dioxide also published in your issue of Oct 10 If this is the case the danger to health from fog will not be removed by the establishment of smokeless zones by the burning of solid smokeless fuel, or by the use of electricity (Gas from which sulphur has been largely removed, is in a different category) *Indeed it* may well be that the greatest single factor increasing danger from fogs in London lies in the erection of vast new power stations in the Metropolitan area

Since all solid fuel commonly consumed whether in industry at power-stations or on domestic hearths, contains a greater or less proportion of sulphur the only way in which the emission of oxides of sulphur into the atmosphere can be reduced short of installing elaborate plant for washing flue gases, is by reducing the consumption of fuel

In the domestic sphere this has already been done in that the present annual domestic consumption of solid fuel has, as a result of restrictions been reduced by about 15 million tons, compared with the pre war figure Over the same period coal burnt in electric power stations has increased by some 20 million tons.

It is high time that the indictment of the coal burning domestic grate as a major cause of atmospheric pollution should be critically re-examined While the supply of smokeless fuel remains at a substantially unchanged level, the main effect of the creation of smokeless zones will be to shift the incidence of smoke from one part of the country to another In the process, their establishment will not significantly reduce the amount of sulphur oxides discharged into the atmosphere

ERIC BELLINGHAM
Director-general,
Coal Utilisation Council.

London S W 1

THE WRONG BLOOD

SIR,—Your leading article of Aug 1 discusses accidents in blood transfusion To illustrate their causes you give five examples of human carelessness—I should myself call them administrative mistakes'—but only one example of a technical error by an uninstructed technician *It strikes me therefore as a little illogical to insist* that 'transfusion must be under the direct control of a senior pathologist Of course I appreciate the implied compliment to senior pathologists—that they alone are reliable enough to be trusted with such things But I still feel that since blood *transfusion* is a form of treatment it should be left to a clinician The pathologist should administer the blood bank but otherwise he should be responsible only for grouping and matching He might well use the following formula for his report

> "The red blood cells obtained from a sample of blood labelled with the name received at
> on have been tested and found to belong to group Serum from the same sample of blood failed to agglutinate red cells from (a) bottle(s) of stored blood of group numbered "

and there his responsibility should cease

Pathological Department,
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London, E 11

W W WALTHER

BACKFLOW IN RETROGRADE PYELOGRAPHY

SIR,—I was very interested in your annotation (Sept 19) on this subject, which was discussed at the annual meeting of the British Association of Urological Surgeons in Edinburgh in 1951, and was reviewed last year[1] The findings agreed in the main with the subsequent work of Kohler[2] to which you refer but there are some points which, I think, merit discussion

You state that in retrograde pyelography backflow, or penetration of contrast medium beyond the confines of the renal pelvis, has been estimated to occur in anything from 4 to 25% of examinations This figure is perhaps rather high In 1876 reports of retropyelographic examinations, I found it in only 2%[1], and in a further personal series of 547 retrograde pyelograms in 282 patients, I have found the same percentage—2 This is a much lower figure than Kohler's 154 cases of backflow in 628 routine retrograde pyelograms

Pyelorenal backflow is essentially a traumatic, pressure phenomenon, leakage of the contrast medium injected up the ureter occurring at the calyceine fornix angle into the renal sinus fat and into the tributaries of the renal veins, as has been shown by the investigators mentioned in your annotation, and particularly by Hinman[3] Many urologists, therefore, when injecting contrast media up the ureters use a funnel and rubber tube and run it in by gravity The pressure used in injecting with the hand syringe is surprisingly high, and Hinman and Redewill[4] noted how easy it is to produce high pressures—even up to 200 mm Hg—very quickly You mention that Kohler describes his findings in 27 patients in whom he performed retrograde pyelography, recording the pressure in his syringe with a manometer in circuit I have now records of 547 manometric readings in 282 patients (142 males, 140 females) My findings are very similar to Kohler's Pain is not a reliable guide to the state of filling of the renal pelvis during retrograde pyelography Some patients tolerate pressures of over 100 mm Hg without discomfort, some have severe discomfort at 20 mm The appearance of backflow is a variable phenomenon, occuring at a pressure as low as 25 mm Hg, and pain may or may not accompany it

Kohler divides backflow into three types (*a*) sinus extravasation, (*b*) pyelotubular backflow, and (*c*) a mixture of the two He also mentions the streaks passing medially from the kidneys, seen in some pyelograms These appearances were originally considered to be due to pyelovenous backflow, but Higham[5] pointed out that they were more likely to be lymphatic Kohler and the majority of other modern observers tend to think that most of the published cases are, in fact, examples of lymphatic spread They continue to be, however, something of a puzzle

It is, as you mention, quite easy to inject the renal vein via the ureter in cadaver specimens, and a cast of the renal vein is readily obtained by injecting 'Neoprene' into the renal pelvis That being so it is reasonable to suppose that, in some of the cases showing fine streaks passing medially from the kidneys in certain pyelograms, the appearance is due to venous backflow, particularly as the arch shaped streaks seen running between the calyces are usually prominent in these cases The arch shaped streaks are usually taken to be dye actually in the arcuate veins, which lead to the main renal vein

On the other hand, the "beaded" appearance of of these streaks, and their position—passing in front of the lumbar transverse processes—strongly that they are lymphatic channels Kohler's observ the appearances persisted in his cases for three to five and that there was no fluorescence at all in those patients were tested, tends to confirm the "lymphatic" view K use of fluorescein sodium with the contrast medium is a most valuable contribution to the investigation of phenomenon Until lymphatic channels can be dem demonstrated by dissection in injected cadaver sp however, there will remain some doubt as to t or causes, of the appearances

In this country Williams[6] distinguished the vari pyelorenal reflux from the radiologist's point of view (1) pyelovenous, (2) pyelolymphatic, (3) pyelotubular (4) pyelo interstitial extravasation Combinations of varieties may occur in the same case This classifi more comprehensive, and more useful, I think, than th

The possibility of backflow in retrograde pyelo should warn all those performing this investigati inject the opaque medium up the ureter as gen possible into that really porous organ, the kidney Ogier Ward made a particular point of this in F Moore[7] has described some of the more serious co cations arising from this investigation, but the degrees of penetration of the medium beyond the c show how easy it is to damage the kidney Gent pays therefore, and the more careful one is forming retrograde pyelographic examinations, the cases of backflow will be seen The subject of pyel backflow is of great interest, and is linked with problems of renal physiology and pathology— nephrosis, for instance There is plenty of sco further research here

Edinburgh

JAMES A R

EMPLOYMENT OF THE DISABLED

SIR,—Your annotation of Sept 19 leads me to m the results of a small survey on disabled young w conducted in Birmingham;[8] among 54 firms and co 140 disabled young people, which contrasts to extent with Ferguson's findings in Glasgow[9]

In 1951, Birmingham, in a period of full emplo offered a wide and varied selection of work opport in light industries Disabled young people (exc epileptics) had no more difficulty in finding jobs their able bodied counterparts During this p disabled young people were able to change their j working conditions were unsuitable, and in fact d hesitate to change jobs for more trivial reasons therefore not surprising to find that, although in half of those leaving their jobs the reasons given connected with their disabilities (such as uns work, nervous strain, and noise), only one young was found actually to be doing work unsuited t physical capacity He had taken his job without th of the Youth Employment Bureau and without acq ing his employers with the fact that he suffered cardiac disease

On the other hand the inadequate number of di young people receiving suitable training in B certainly bears out the Glasgow experience out of 140 were actually apprenticed, of 31 in tra the boys were engaged in the electrical, optical, glass jewellery trades and the girls in dressmaking embroidery Of both sexes 36 were engaged in cl work, the others were in semi skilled jobs limited prospects of advancement Of 11 firms t survey which had apprenticeship schemes, 2 had accepted disabled youngsters and 4 more were wi take them Of the 5 firms which refused, 4 did so

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1 Ross J A. *Brit J Urol* 1952, 24 27
2 Kohler R. *Acta radiol Stockh.* 1953, suppl 99
3 Hinman, F *Surg Gynec Obstet* 1927, 44 592
4 Hinman, F Redewill F H *J Amer med Ass* 1926 87, 1287
5 Higham A. R. C. *Brit. J Surg* 1937, 25, 139

6 Williams, E R. *Brit J Radiol* 1941, 14 275
7 Moore, T *Brit. J Urol.* 1939, 11 233
8 Walton C *Social Service* 1953, 27 73
9 Employment Problems of Disabled Youth in Glasgow memorandum no 28 H M Stationery Office 195

considered the work was unsuitable for disabled le and the 5th (a light engineering firm) because led people would not be able to join in with the l activities of the apprentices school

e money time and skill spent on medical reablement special education of the young disabled is wasted s the youngster is settled in suitable work and the training he needs if he is to get through his ing life without becoming a burden to himself or tate More training and apprenticeship facilities in ble industries should be made available to the g disabled school leaver—if necessary, by legislation

University Edgbaston
Birmingham 15

CYNTHIA WALTON

FREEDOM TO PRESCRIBE

—Your annotation of July 25 has been brought o notice of the Northern Ireland General Health ces Board

e Board are in full agreement that matters of public est and matters affecting the public purse should be presented to the public and it has, therefore always the policy of the Board to afford full opportunity to sentatives of the press to attend Board meetings and t such matters This policy was not departed from e case to which you refer Your annotation was, ver based apparently on articles which appeared in ress on June 25 and which reported only the dis on at the Board meeting on the previous day and ot give the full picture up to that date

u will appreciate that from time to time matters for discussion the publication of which at that might be undesirable and it is, of course the ice to consider such cases in camera. All Board Committee minutes when confirmed are however available to the press and the only matters which xcluded from the minutes for this purpose are those h are clearly unsuitable, in the interests of the ces, for publication

pursuance of this policy the decision of the special mmittee was discussed in camera but was made able to the press in the minutes of the meeting of the d at which the discussion took place I am not e that the decision was published by the press and, our information, it was to the effect that the Committee were satisfied that the Board, in acting upon the o of their professional committees and in accepting the decisions of the Central Medical Committee had taken the only action possible in the circumstances

The Board have instructed me to furnish you with the accompanying statement giving some examples of the prescribing of Anahæmin ' 'Examen and Oral Liver Extract by the doctor concerned. In accordance with regulations in Northern Ireland it is the Board s duty to submit to a statutory Committee nominated by the medical profession here and known as the Central Medical Committee cases of apparently excessive prescribing The Board having regard to the views expressed by the Medical Research Council and the manufacturers of anahæmin have felt bound from time to time to regard this doctor s prescribing as in excess of what was reasonably required for the treatment of his patients They accordingly submitted cases to the Central Medical Committee which committee after investigation and having afforded the doctor full opportunity to justify his prescribing determined that the prescribing was excessive and assessed the amounts of excess These amounts have been recovered by the Board from the doctor

Northern Ireland General Health Services
Board 9 Upper Queen Street
Belfast.

G D STEWART
Secretary

Quantity		Period (days)	Approximate daily dosage		Cost	Amount recovered from doctor
Anahæmin or examen (ml.)	Oral liver extract (oz.)		Anahæmin or examen (ml.)	Oral liver extract (oz.)	£ s. d.	£ s. d.
610	—	10	26 84	—	40 2 9	40 2 9
1625	400	227	7 16	1 77	2[illegible]3 1 11½	211 0 1
2340	24	44	53 2	0 51	190 8 3	182 5 10
600	72	66	9 2	1 1	57 13 8	54 18 2
1950	—	36	55 71	—	174 18 8½	—
950	—	13	73·07	—	85 7 8	—

above cases A B and C, were heard by the Central Medical ittee, who decided that the prescribing was excessive and mined the amount of the excess. In case B the doctor appealed ependent referees appointed by the Ministry of Health and Government who upheld the decision of the Central Medical ittee Cases D and E have not yet been decided by the al Medical Committee

154 of the doctor's prescription forms dispensed in July by ts in his area, 87 or 56½% were for liver preparations

e figures exclude the charges payable by the patient and present the net cost to the Board

EFFECT OF PENICILLIN ON PINK DISEASE

SIR,—In each of the following two cases penicillin seemed to have a striking effect on pink disease

CASE 1—A girl aged 13 months, was first seen on Aug 8 1951 with bronchopneumonia and pink disease She had previously been diagnosed as a typical case of infantile acrodynia at the Royal Hospital for Sick Children Glasgow with a history dating from May 2 1951

The child was thin listless and miserable and remained in the position associated with pink disease There was diffuse bronchopneumonia and typical eczematous lesions of glove and stocking distribution. Distaquaine penicillin was given intramuscularly for six days, and Anthisan cream was applied locally to hands and feet

CASE 2.—A girl aged 2 years 11 months was first seen on Nov 25 1951 On Dec. 5 she was treated with distaquaine penicillin for an incidental throat infection, after which her general condition appeared to improve Subsequently she was admitted to Weymouth and District Hospital where the diagnosis of pink disease was confirmed Because of the general improvement after the penicillin therapy for tonsillitis oral penicillin 200 000 units four times daily was commenced on Jan. 8, 1952 and continued until Jan. 21

Both these cases conform with the classical description of pink disease [1] and both improved considerably during and after penicillin therapy The patients appeared normal on cessation of treatment and have since remained so

Chloramphenicol is reported to have brought about apparent cure in two cases of pink disease [2]

It is known that antibiotics may improve the availability of vitamins of the B group: megaloblastic anæmia of pregnancy has been successfully treated by penicillin alone [3] and aureomycin can increase the availability of vitamin B_{12} administered orally in cases of pernicious anæmia [4]

Antibiotics may alter the intestinal flora for example aureomycin in high doses can effectively remove bacteria from the human gut [5] and dietary streptomycin has been shown to cause an increase in *Bacillus megatherium* (known to synthesise vitamin B_{12}) in the gut of the mouse [6,7] Penicillin prevents depression of growth in poultry probably by altering the bacterial flora and

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1 Price, F W Textbook of the Practice of Medicine. London 1950; p 385
2 Cook A S. *Brit med J* 195* i 383
3 Foy H, Kondi, A Hargreaves, A. *Ibid* 1951 i 350
4 Lichtman, W, Ginsberg V., Watson, J *Proc Soc exp Biol., N Y* 1950 74 884
5 Dearing W H W., Heilman F R. *Proc. Mayo Clin* 1950 25, 87
6 Lewis, J C., et al United States Department of Agriculture Bureau of Agricultural and Industrial Chemistry 1949 *AIC 254*
7 Smith D G Robinson, H J *J Bact.* 1945 50 613

promoting the growth of bacteria that synthesise growth factors, or eliminating bacteria that destroy growth factors[8]

We wonder whether the penicillin may have acted in a similar manner in these two cases of pink disease, with the consequent absorption of some previously missing vitamin factor

Evershot, Dorset.

R J DAVIS
B S C GASTER

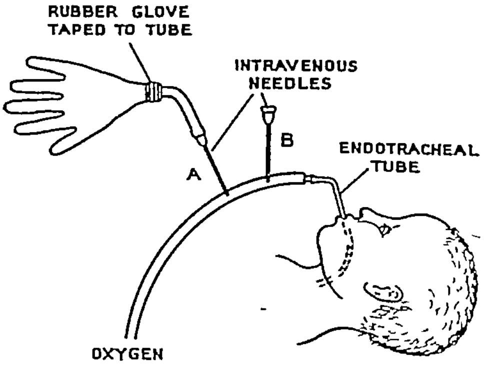
ASPHYXIA IN THE NEWBORN

SIR,—For the immediate and certain relief of asphyxia of the newborn, endotracheal intubation followed by inflation, using a rebreathing bag, is a method which is not, I think, used sufficiently

It is wise to remember, as Eastman[9] has pointed out, that "in the presence of anoxia, apnœa is resistant to all types of treatment other than correction of the anoxia itself Even convulsive doses of nikethamide have no effect on anoxic apnœa, on the other hand, a few insufflations of oxygen produced immediate breathing"

Quite often, however, there is a mechanical barrier in the way of the all important oxygen Sometimes this takes the form of a thick matted curtain of mucus I feel that endotracheal intubation is justifiable only after pharyngeal toilet has been carried out under direct vision Quite often this mucus barrier can be demonstrated at this stage Pharyngeal toilet has to be done anyway, as the intubation is completed under direct vision

If it does nothing else, laryngoscopy of the newly born demonstrates the futility and inefficiency of the mucus catheter in common use A good deal of misunderstanding appears to exist about the trauma involved in this procedure of intubation Naturally the disturbance is a matter of degree and is related to the skill of the operator A size 0 tube is used, either all rubber or armoured with a wire spiral embedded in the rubber Plastic tubes are easier to introduce, but the fairly thick walls of the tube reduce the lumen



Semiclosed circuit for insufflation of newborn

Writing on artificial ventilation of the lungs, Professor Pask[10] evidently prefers efficient artificial respiration to inadequate spontaneous respiration, for he remarks "Positive pressure ventilation can be carried out without causing disturbance in the cardiovascular system"

Let it be stated quite clearly that there is less shock—much less—than in other methods of artificial respiration Even using a mask alone, considerable force may be used to blow oxygen past an obstruction Intubation is greatly facilitated by a cunningly contrived inclined plane, and the infant need not be exposed, but can be kept well wrapped up

Anoxia at birth is a common cause of small cerebral hæmorrhage—to mention only one result of asphyxia—but it is for the neurologist to assess the late anoxia Nevertheless, the obstetrician is present the neurologist is not, although the latter appreciate more acutely the significance of anoxia though it only lasts a short time

Very occasionally it has been necessary to inflation, at least at intervals, for some time. accompanying figure shows an arrangement which be used when the normal equipment of the machine is not available An ordinary surgeon's makes an excellent rebreathing bag, it is attached rubber tube and sealed with adhesive tape A large needle is needed at A, otherwise an incorrect is imparted to the "bag" The other needle simply a blow-off valve to dispose of carbon dioxide

The most significant clinical feature after through an endotracheal tube is the bright pink the hands and feet which can be achieved few minutes of insufflation

Obviously a device of this kind is easily worked the type of pneumoflator described by Dr Beaver[11]

Watford Maternity Hospital

J NOEL J

POSTURE, BACKACHE, AND HEALTH

SIR,—Few people, even trained athletes and of the Armed Forces, understand the essential of muscle movement and joint control May I attention, for example, to some remarks made months ago (May 1) by The Doctor in one of the he broadcasts on Friday mornings? Speaking backache, he said

> "But fortunately many ordinary backaches are or relieved by the same quite simple measures. The important thing is to maintain the hollowing of the part of your back When standing, stick your out backwards, brace your shoulders back and your back muscles, even if this does mean sticking stomach out a bit"

In saying this The Doctor was advising his to maintain a hollow back by contracting the erector group of muscles Another school advises slight of the spine, favouring a neutral position with the down" instead of projecting the buttocks back

Now our bodies are composed of four main entities attached to fixed parts (a) the head on and trunk, (b) the arm and shoulder girdle on the wall, cranium, and cervical and dorsal vertebræ, trunk on the pelvis, and (d) the whole body attached to the ankles and feet For a movement of the part to be efficient, it must be performed on a firm produced by the active contraction of the prime muscles If in standing a person has all the fixor muscles alerted he or she will adopt a more ape like stance which includes relative flexion of lumbar spine with slight flexion of all other joints

There are three ways of sitting or standing

Inactive —The person slouches or sags, thus the mobile part of the body to put a constant strain the fixed parts

Passive —This is the position of standing The advocates Sagging and forward-flexion strain lumbosacral junction is prevented by placing the of the trunk backwards and making the back through contraction of the erector spinæ muscles position, however, does not fix the lumbosacral lation except by imposing a chronic strain apophyseal joints, which in time tends to osteo-arthritis

Active —This is the ideal First of all the neck as long as possible with the chin tucked in and in a posterior direction Thus the head, on straightened neck, is placed evenly between the in both coronal and sagittal planes The girdles are held up and against the chest consciously neither forwards nor backwards ominal muscles are contracted upwards with the ocks tucked under and knees very slightly bent

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[8] Coates M F et al. *J Sci Fd Agric.* 1952, no 1, p 47

[9] Eastman N J *Amer J Obstet Gynec* 1940 40 647

[10] Pask E A *Brit med J* 1953 1 1048

[11] Beaver, R. A *Lancet*, 1953, i, 977

active standing the weight of the body is ed evenly on the heel and outer side of the foot, ging the toes into the action of standing In this ure the anti gravity muscles are pulled up so that weight of the mobile part is not acting as a strain he fixed part the other muscles are in balanced raction and there is therefore no suggestion of ion If one learns to stand like this continuously never seems to get tired, and the ageing process of and tear is slowed down Physically the body is state of readiness to accept strains arising from its ronment: the person thus prepared becomes what may call a physical extravert

children were taught this posture at an early age would grow up in the physical attitude of alert unconsciously maintained, and there would be fewer lled accidents Furthermore, fewer people would r from disorders such as fibrositis and osteo arthritis h faulty posture helps to produce A good posture ld in fact be the *concern not only of orthopædic* ons, who are trying to correct disorders but of all want to promote or achieve health

idon W 1 W E TUCKER.

‘CHEMOTHERAPEUTIC AGENT’ AND “ANTIBIOTIC”

R,—According to Dr Erwin (Aug 20) chemo py covers treatment by chemical agents and the ble aspirin is of right a chemotherapeutic agent Erwin says that when chloramphenicol was syn sed the use of the term antibiotic to mean a mical substance produced by micro-organisms sman) became obsolete and chemotherapeutic t’ and antibiotic have come to mean the same By this token are we to regard aspirin as an iotic?

e Town South Africa M GLASS

OLINE IN THE TREATMENT OF EPILEPSY

R,—In this colony for epileptics, we have treated t 60 patients with Mysoline’ since September Only 31 however 18 females and 13 males, have observed long enough to evaluate the results Their ranged from 1 to 57 years and the duration of their *s from 1 to 47 years. 24 of the cases capable of* sment were classified as idiopathic and 7 as sympto 24 suffered from both grand mal and petit mal m grand mal alone and 2 from petit mal alone.

e doses of mysoline varied from 0 25 to 2 g daily he commonest dose was 1 to 1 25 g daily Patients started with 0 25 or 0 5 g daily, and the dose was ased once or twice a week A thrice daily dosage ne was commonly used.

soline was used alone in only 2 of the severe cases ilepsy The rest had in addition either phenytoin, oin (‘Mesantoin’) phenobarbitone or Citrulla or a combination of these drugs

7 cases the fits were completely or almost completely olled in 9 there was a significant reduction in umber of fits; in 4 only major attacks were controlled little or no reduction in the number of petit mal ks; and in 1 the number of petit mal attacks ased

soline was more effective against grand mal than mal No difference could be seen in the effect on the athic as compared with the symptomatic, cases ovement was noticed in the mental well being of 10 nts whose fits were controlled They showed less iness and drowsiness and greater initiative

le-effects were seen in 9 patients who showed lent giddiness and sleepiness at the beginning of treatment In 1 patient giddiness and ataxia were quite severe. None of the patients had skin eruptions

The blood and urine of all patients were examined regularly and the only abnormality found was leucopenia in a patient who had shown the same response to earlier treatment with Dimedion’ methoin, and ‘Epidon. Treatment in this case was discontinued

Kolonien Filadelfia,
Dianalund Denmark GUNNAR JORGENSEN

DOSAGE OF ANÆSTHETICS

SIR —In his letter of Oct 3 Dr Galley draws attention to the greater sensitivity to intravenous anæsthetics of the Asian patient as compared to the European In my early experience with Arab patients in the University Hospital in Damascus I was very much impressed by the extreme *variability* in the response to intravenous anæsthesia which made the utmost caution necessary in its use

It soon became apparent however that this variability was due to the existence in the hospital population of three groups of patients with distinctly different ways of life

(1) *The Bedouins: hardy frugal non-smoking and non* drinking nomads in whom arteriosclerosis hypertension peptic ulcer and other diseases of stress are extremely rare This group requires very much less intravenous anæsthetic than the average European it is a particularly dangerous method to use in emergency surgery on Bedouin patients.

(2) The Arabs of the city in this group the habit of life in these days approximates very closely to that of the European and the response to intravenous anæsthesia is not apparently different

(3) The Arabs of the villages: a group in which mal nutrition is common and the hardiness of the Bedouin is lacking addiction to both alcohol and tobacco is not unusual The response to intravenous anæsthetics is intermediate between the two *previous* groups, but cases of excessive sensitivity occur fairly frequently

It must be observed that there are no ethnological differences between the three groups and variations in response to anæsthesia must be the result of factors associated with their differing habits of life The identification of these factors offers an interesting field for research

Our experience with muscle relaxants is that there is no variation in response corresponding to that found with intravenous anæsthetics, although the immediate impression is of an over-all sensitivity greater than that found in Europeans. It has become apparent however that the Arab patient requires approximately the same dose of both Flaxedil and *d* tubocurarine to produce the initial curarisation, but that the duration of effect is appreciably longer than in the European This means a slower rate of elimination and my impression is that in this respect there is not nearly as much variation between the extremes in the groups mentioned above as might be expected from the variations in response to intravenous anæsthesia. We have used Scoline in over 200 cases in patients from all three groups without discrimination and although we have had 1 case of apnœa lasting three hours, the response has otherwise been uniformly the same as with European patients and the dosage required has not been less

While the majority of Arab patients are easy subjects for anæsthesia there is one type of patient which in my experience is more difficult to deal with than any encountered in Britain not excluding the chronic alcoholic and that is the hashish addict These patients combine a resistance to intravenous anæsthesia so great that 2 g of thialbarbitone (Kemithal) given quickly produces no more than drowsiness with a respiratory tract so irritable that the inhalation of any gas causes uncontrollable coughing I find the only way of dealing with them even for minor operations, is to give a full dose of *d* tubocurarine to which their resistance is normal and to force as much cyclopropane into them as possible during the apnœic phase The patients must be watched very closely after operation, for the recovery stage, even after cyclopropane, is invariably most inelegant, with much laryngeal spasm, coughing, and cyanosis In Damascus, hashish addiction is a positive indication for local anæsthesia where this is at all possible

Department of Anæsthesia,
Syrian University, Damascus L T SCOTT

SIR,—From three years' experience in the late war as anæsthetist to a combined British Indian military hospital I can confirm Dr Galley's findings regarding dosage of short acting intravenous barbiturates in Indian and Oriental patients

The average amount required for induction of anæsthesia is about two thirds of that needed in a corresponding European My initial ignorance of this fact nearly resulted in an unpleasant surprise!

I note that in his letter last week Dr Clement advocates Lake's technique for high and mid spinal levels, where spinal analgesia is the method of choice, mentioning that only 9 ml of 'Light Nupercaine' will give satisfactory results for upper abdominal surgery in patients of average size While this is true, I feel that this technique is rather more exacting and less comfortable than methods employing 'Heavy Nupercaine,' using the equivalent of only 4 mg more of the drug

As Professor Macintosh has pointed out,[1] the good and bad effects depend not on the administration of 10 or 15 mg of nupercaine, but on the level within the dural canal reached by the drug

Maidstone A W H ASHBERY

PERIODIC MEDICAL OVERHAUL

SIR,—I was interested in Sir Adolphe Abrahams's points of view (Sept 26) and would agree with him that during medical examination emphasis should be placed on health-mindedness rather than on the possibility of disease I cannot, however, accept so heartily the suggestion that health guidance is not a matter for the doctor and should be handed over to someone else

Unfortunately it is all too true that the training of the medical student and the young graduate has not provided "the best milieu for health-mindedness" The reason is not far to seek it is that teaching has been conducted almost exclusively by specialists in *diseases* of various groups of systems and parts of the body One could scarcely expect people preoccupied with disease processes to think in terms of "health." Surely, however (and particularly in view of the altered scene resulting from the National Health Service), health should be the prime concern of family doctors and of all who have to deal with individuals as "whole beings"

The trend is for specialism to be carried into ever-narrowing fields, and it would seem that there is need for introducing at some stage of the curriculum a study of health as what might be termed a "positive factor" There is no room for complacency in regard to the health of the nation as a whole No medical man walking along the streets of any of our large towns and taking stock of the men and women between the ages of thirty and forty (when they should be at their prime) could fail to be impressed by the number who are already losing health and vigour Probably not many of these people would say that they were ill or in need of medical attention, but most of them would certainly benefit from judicious health guidance

I am not in favour of health education in bulk, since I am not sure that much of the propaganda being put across to the public is either of value or harmless Health is normally a matter for individual advice, as and when required, but in my view periodic "health" examinations carried out in each decade of life and in proper surroundings by a doctor would serve a useful
and would amply repay time and money spent
It would be wrong to suggest to the public
examinations would adequately safeguard
or even most, of the ills to which flesh is
heir, though even if limited to a physical
they would have some predictable value T
of a net to catch disease would, however, be
of their function The main purpose would be
the standard of health and when this was found
low to search, as with disease, for the cause
search would involve many factors heredity
background, personal habits and interests,
general environment, and of course the
disease processes

The value of such examinations would
limited to the individual, for the findings, if
recorded and filed, would provide extremely
information for those entrusted with the nation'
—information of no less, and probably much
value than that provided by morbidity figures.

Student Health Service,
The University, Aberdeen H A.

CASSETTE HOLDER FOR USE IN THE OPERATING-THEATRE

SIR,—Reversal of the X ray tube and cassette
the operation for pinning a fracture of the
femur, as practised by Mr Le Vay (Sept 12),
solve the irradiation problem Most orthopædic
are not equipped to take a cassette between the
legs, and the cassette is *held* in position by the
Moreover, this technique necessitates an X ray
on the "operating side" of the patient—an a
disliked by most orthopædic surgeons and all
sisters, especially when only one X ray
available—and it frequently has to be moved in
take the anteroposterior and lateral views of t

The cassette holder I described (Aug 29)
surgeon from X ray irradiation and can be used
other orthopædic procedures in which X ray
desired

I do not doubt that Mr Le Vay obtains
films It is only fair to point out that the
films obtained using either a curved cassette
necessary in Mr Le Vay's method) or an
cassette, depends on the experience of the
and the quality of the X ray tube

Kent and Canterbury Hospital,
Canterbury MARK L.

CŒLIAC-PLEXUS REFLEX IN MAN

SIR,—A very similar reflex to that discussed
B H Smith (Aug 1) occurs spontaneously
pregnancy, probably as a result of fœtal c
the structures related to the solar plexus.

While at Maternidade Escola (Universidade do
Rio de Janeiro) I observed five pregnant women
exhibited a distinct and progressive fall in blood
leading to circulatory collapse when they
dorsal recumbent position[1] McRoberts
similar cases, and named the disorder "postural
The postural circulatory collapse in pregna
evidently of a reflex nature, in two cases I fo
it was absent after paravertebral block I ha
noticed that atropine in a dose of 1 5 mg (gr
intramuscularly averted the fall in blood pressure
this drug was given in smaller doses it only
the reflex or delayed its appearance As Dr
points out, the action of atropine contradicts the
concept that the solar reflex is caused by
otonia—unless perhaps it could be proved

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[1] Macintosh R R. Lumbar Puncture and Spinal Analgesia Edinburgh 1951

[1] de Rezende, J M. *Arch. bras Med* 1950, 40, 315
[2] McRoberts, W A. jun. *Amer J Obstet Gynec.* 1951

a sympathetic nervous system contains depressor ergic fibres as in the dog [3, 4] easured the venous pressure in two of the patients here was a decrease parallel to the fall in the al blood pressure, although of lesser degree This ccords with the suggestion of Gordh [3] that stimula f the solar plexus might lead to loss of tone of the veins.

hypothesis put forward by Dr Smith to explain lar reflex—that it is due to vagal cardiac inhibition onsequently diminished force of contraction of the muscle—is a very attractive one but needs further n its favour

Ioffre Marcondes de Rezende

Vista, Matto Grosso,
Brazil.

IOMYELITIS WELSH REGIONAL BOARD AND MINISTRY OF HEALTH

—It is regretted that the British Orthopædic ation should have gained the impression as ted in Sir Reginald Watson-Jones's letter last that orthopædic surgeons are in any way excluded heir rightful place in the treatment of poliomyelitis les It is only fair to point out that the special ittee of consultants which met some time ago were g essentially with one aspect of poliomyelitis— f the respiratory complications

recommendations in the memorandum to which eginald refers, are additional to the already existing ements which are described and which make special on of the necessity for orthopædic supervision

A Trevor Jones
Senior Administrative
Medical Officer

h Regional Hospital Board
Cardiff.

CARDIOSPASM

—Your leader on this subject (Aug 15) does not on the comprehensive contributions of Irwin [6, 7] and Brown Kelly [8] These include many ations of museum specimens, all of which fail eal any organic stricture at the cardia, even where s gross œsophagectasia. The first necropsy specimen liospasm was described by Cruveilhier in 1821

y facts favour a neurogenic origin—i e., paralysis ng in particular the longitudinal musculature of sophagus ('the inhibition of contraction of the udinal coats' of Einhorn and Rolleston)

lov (1887) in his classic experiment in the dog showed ect of section of both vagi and demonstrated paralysis lower third of the œsophagus with the cardia only ll as a result of which not all the swallowed food could to the stomach but would stagnate in the lower part œsophagus; the frequent vomiting would exhaust the [9] This work of Pavlov's was carried out before the ry of X rays

erg [10] repeated Pavlov's experiment in the cat Bilateral my produced tightly constricted sphincters at the upper wer ends of the œsophagus. He demonstrated radio cally that an opaque meal introduced into the œsophagus n an animal became trapped there. If the animal was ded by the head the opaque meal was held up at the if suspended by the tail the meal was held up at the haryngeus. Paralysis of both recurrent laryngeal results in achalasia of the crico-pharyngeus.[11, 12] This is ted also in poliomyelitis

ght and Adamson [13] found that stimulation of the vagus ed relaxation of the cardia and that stimulation of the sympathetic produced contraction They also found that excision of the vagus produced the clinical and radiological picture of achalasia when the vagus and the sympathetic were excised there was no obstruction at the cardia. Brown Kelly [8] *and Rake [14] showed that there was destruction of the* nerve elements in Auerbach's plexus

Entalacão (known as tropical cardiospasm tropical dysphagia or *mal d'engasgo*) is a disease characterised by recurrent attacks of severe difficulty in swallowing It is confined solely to certain geographical regions of South America Gray [15] drew attention to this type of mega œsophagus and confirmed its peculiar geographical distribution. He attributes the cause to avitaminosis but in its distribution it acknowledges no economic barrier The cause is probably viral (akin to poliomyelitis) This produces paralysis of the longitudinal muscles of the œsophagus, the contraction of which plays an important part in the opening during deglutition, of the normally closed cardia

Much has been written on what opens the cardia (or for that matter the crico pharyngeus) but little on *how* each is opened If a thin walled rubber tube of wide calibre has in its course a constriction, closing its lumen (as a sphincter) it may be opened by stretching—i e., in the same way that the bulge of a de Pezzer catheter is flattened out by stretching Contraction of the longitudinal muscles of the œsophagus will open the cardia in the same way contraction of the oblique fibres of the constrictors opens up the crico pharyngeus by its longitudinal pull Thus paralysis of the longitudinal musculature will result in cardiospasm and a correct appellation of this condition is paralysis of the longitudinal muscles of the œsophagus.

Occasionally carcinoma of the cardiac end of the *stomach will hamper the contraction of the* œsophageal musculature and prevent the opening of the cardia. As a result from time to time there develops great dilatation of the œsophagus with vigorous peristalsis visible on screening Radiologically this simulates cardiospasm [16] The dilatation passes off but returns at intervals This intermittent cardiospasm may be for many months the first and only indication of the presence of cancer of the cardiac end of the stomach Ogilvie [17] and Park [18] have noted this association

London, W 1 N Asherson

Public Health

Pneumoconiosis

The National Coal Board and the National Union of Mineworkers have made plans for a survey of pneumoconiosis in British coalfields.[19] One of the aims of the survey which will be conducted in collaboration with the Medical Research Council will be to discover the safe limit of dustiness in which miners can work without danger to their health A mobile unit with X ray equipment will visit 21 pits throughout the country and it is hoped that every person employed in these mines will be examined The 24 pits have been selected as representative of the various conditions found in British mines. The mobile unit working from Edinburgh will make a start soon and another from Cardiff will do so later

Poliomyelitis

Poliomyelitis notifications (uncorrected) in England and Wales during the week ended Oct. 3 (39th week of *the year) were (previous week in parentheses) : paralytic,* 79 (119); non paralytic 78 (99), total 157 (218).

The reduction in notifications of 40 paralytic and 21 non paralytic cases is satisfactory and there is no doubt that the drop to the winter levels of the disease is under way

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Obituary

EDMUND BRITTEN JONES

Kt., M A Oxfd, M B Adelaide, F R C P, F R A C P

Sir Edmund Britten Jones, who died on Sept 30 at the age of 64, was one of Australia's leading physicians Educated in Adelaide, he graduated in 1910 and was selected as South Australian Rhodes scholar for 1912 During the first world war he served with the Australian army medical service in India, and on returning to South Australia settled in suburban general practice for a few years In 1926 he came to England and obtained the M R C P, and when he went back to Adelaide he entered consultant practice He was elected to the staff of the Adelaide Children's Hospital, but by a combination of circumstances he was never appointed to the staff of the Royal Adelaide Hospital, and he was thus one of the relatively few consultants who have attained eminence without being attached to a general hospital After a period as honorary medical secretary, he was elected president of the South Australian branch of the British Medical Association for 1933–34 At the outbreak of the late war he at once joined the army, and served in the Middle East in command of the medical division of the 2/2nd Australian General Hospital He was elected F R C P in 1942, and in the same year returned to civilian practice where he worked extremely hard and found that his services were greatly sought after on committees and boards In 1944 he was elected to the council of the University of Adelaide and to the council of the Royal Australasian College of Physicians, of which he later became a vice president He served on the Medical Board of South Australia for several years, and was elected its president in 1950 He was knighted last New Year

G W P writes "My memory of Adelaide, which I visited as Sims professor in 1949, is of a city more English than the English In its wide streets, spacious squares, and leafy parks life pursued an even, unhurried pace In its Adelaide club lingered the manners and the courtesy of an age now passed in this country In this society the medical profession holds an honoured place, and among its leaders was Teddy Britten Jones, who in many ways typified the society in which he lived Burly of figure, eager of temperament, kind, gentle, and wise, he was a man to whom it was natural to bring troubles or problems of any kind, sure of understanding and sound counsel"

Sir Edmund is survived by a widow, a son who is a doctor, and two daughters

LEWIS GLADSTONE GLOVER

M.A, M D Camb

Dr Glover died on Sept 25 in his 86th year He had been one of the most respected practitioners in Hampstead, and, in addition to his professional duties, he had taken a considerable part in public affairs

Lewis Glover was the son of Sir John Glover, a shipowner He was educated at Highgate School and Cambridge University, where he gained a first in the natural sciences tripos He received his medical training at St Bartholomew's Hospital, qualifying in 1892 After holding house posts at the Royal Hospital for Diseases of the Chest, City Road, the Victoria Hospital for Children, Chelsea, and St Bartholomew's Hospital, he studied for a few months in Vienna He then settled down in general practice in Hampstead, at that time a rapidly growing suburb The Hampstead General Hospital was staffed by general practitioners, and Glover served on the staff with acceptance, but he withdrew in 1907 when the whole staff became of consultant status After thirty years of general practice, of which he was one of the best exponents, he retired, not to rest, but to take a more active part in his other interests

He was for fifty years a faithful member of the British Medical Association, being at one time president of the Hampstead division, at another vice-president and treasurer of the Metropolitan Counties branch, and for the years 1934–38 a member of the council of the association He devoted much time to local politics, and he was mayor of Hampstead from 1936 to 1938

He was a man with deep religious convictions, and t[illegible]rk which was probably nearest his heart was the help he gave to the Royal Medical B on the committee of which he served for over years From 1932 to 1944 he acted as treasu Fund, and until comparatively recently he attend the committee meetings He was also of St Bartholomew's Hospital In spite of deafness and the stress of a surgical operatio tinued to interest himself in these benevolent until he had entered his ninth decade

Dr Glover is survived by his wife and a daughter

FLORENCE RENA SABIN

M D

Florence Sabin died at her home in Denver at the age of 81 She was the first woman to from Johns Hopkins University, the first to teach the first woman member of the Rockefeller Inst the first woman member of the National Sciences She will always be remembered for her experimental and histological studies of the dev of the cells of the blood and of the reaction of t of the body to the tubercle bacillus Techniq she devised—particularly that of studying livi under suitable conditions of temperature and are in use all over the world today for a purposes The beautifully illustrated series of graphs produced by her and her collaborators Rockefeller Institute will be an enduring Though her conclusions on the origin of the red cell—that most controversial of all problems in tology—may not now be generally accepted, the her work gave to contemporary hæmatol immense She preceded Minot and Castle in h mental *approach to problems* that had hither attacked at a descriptive level

In the late '20s callers at her laboratory at feller Institute were welcomed by a kindly and comfortable-looking with greying hair and eyes, obviously working at the bench with her tors The shy young visitor was taken in, shown what was then the exciting "hot box" and made to feel a colleague—something that much in the early stages of research Simon called Florence Sabin "the greatest living scientist and one of the foremost scientists of a Prophecy is rash, but she certainly had a lively on the early stages of experimental cellular patho

EDWIN JOSEPH COHN

M D, Ph D, S D

Prof Edwin Cohn, whose death in Boston at of 60 was recorded in our last issue, was a d figure in American medical science Educated Amherst and later in postgraduate schools in and New York, he came under the influence of L J Henderson, then professor of biological c at Harvard, whose staff he joined in 1917 Henderson's stimulus, he began the study of the chemistry of the proteins which formed th interest of his subsequent scientific career His and personality soon impressed themselves on h leagues, and within a few years Cohn was vir control of an active team engaged in fund investigations on the solubilities and characte some important animal and plant proteins. much of this work was an extension of the Sörensen in Denmark and Hardy in this count both of whom he had worked—but later he deve along more original lines by applying Debye's on ionic behaviour to proteins and peptides.

At the outbreak of the second world war, Cohn recognised the practical significance of the earlie of his laboratory, and at once turned it to accoun development of processes suited to the la fractionation of the proteins of the plasma. through his projected programme of expansion, he and gained the support of the National Research and the American Red Cross The purified produced under his direction soon found wide ap in medicine, surgery, and the prophylaxis and of some infectious diseases Throughout this ver period, however, Cohn never lost sight of the th ations of the flood of practical studies that red from his department.

ediately the war had finished he started to re-plan oratory so that it might return to more funda considerations of protein structure This reorgan on more academic lines in which he was greatly by Dr John Edsall culminated in 1950 in the shment of the University Laboratory of Physical try Related to Medicine and Public Health ; as its director, was given the title of "university or" Chairs bearing this title had been created at d in 1936 for men of distinction not definitely d to any particular department and his appoint o one of these few and select professorships gave very special pleasure Moreover it was a notable stration of the wisdom of President Conant and lows of Harvard in emphasising once again the art that the fundamental sciences have to play in ancement of medicine

In Cohn stimulated and moulded a large number able young colleagues who came to his laboratory ly from America but from all parts of the world d an aversion to empiricism and sought always et his work by *the application of fundamental les.* It is too soon to judge his place in the develop f protein chemistry but it is undeniable that the f his laboratory and his ideas have given a great s to both theoretical and practical research in this of biochemistry A man of his vigorous personality bly provoked controversies, and their repercussions d as the circle of his war time activities enlarged ese will not dim the happy memories of those who with him—of the regular Monday lunches ulnars, and the Christmas parties where all were *air their views without reserve*

cent years Cohn received many tributes from his ountry and from abroad Numerous honorary were conferred upon him by American and Euro niversities, and he was widely recognised by scienti medical societies both for his fundamental chemical eries and for their ramifying applications in blood sion and immunology The contributions made by artment at Harvard will long remain as testimony to ability as a leader of a team of able investigators the foresight of that great medical school in ing studies in one of the most fundamental ns in biochemistry

WEN MACLEAN, of Cardiff, formerly president of yal College of Obstetricians and Gynæcologists, Oct. 13 at the age of 87

Diary of the Week

OCT 18 TO 24

y 19th

DUATE MEDICAL SCHOOL OF LONDON, Ducane Road W 12
Dr Brian Ackner Aches and Pains of Psychogenic Origin.

ITY OF LONDON
(Guy's Hospital Medical School London Bridge S.E.1.) Prof. W Montagna (Brown University U.S.A): Architecture Growth and Differentiation of Skin (Second of three lectures.)

TE OF NEUROLOGY National Hospital Queen Square W C.1
Dr Robert Aird (U.S.A) Recent Work on Epilepsy

IAN SOCIETY
(Talbot Restaurant 64 London Wall E C.2) Sir Heneage Ogilvie Life is Like That. (Presidential address.)

y 20th

POSTGRADUATE MEDICAL FEDERATION
P.M (London School of Hygiene and Tropical Medicine Keppel Street, W C 1) Prof J H Burn, F.R.S. Acetylcholine and Cholinesterase in Heart Muscle

SOCIETY OF MEDICINE, 1 Wimpole Street W.1
Section of Pathology Dr A G Everson Pearse Prof J F Danielli Dr G H Bourne Dr K W W H Walton, Professor Montagna Applications of Histochemical Methods to Pathology

EYE HOSPITAL, St. George's Circus, S E.1
Dr R. D Lawrence Diabetes and the Eye

OF DERMATOLOGY St John's Hospital Lisle Street, 2
M Dr D I Williams Erythrodermias.

FOR THE STUDY OF ADDICTION
(11 Chandos Street, W 1) Dr H K V Soltau: Scope and Effect of Institutional Treatment in Alcoholism. (Presidential address)

Wednesday 21st

ROYAL COLLEGE OF SURGEONS Lincoln's Inn Fields, W C 2
5 P.M Mr L N Pyrah Ureterocolic Anastomosis—Technique Management, and Aftercare

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M. Prof N H Martin: Circulating Proteins in Health and Disease

UNIVERSITY OF LONDON
6 P.M (Guy's Hospital Medical School.) Professor Montagna Architecture Growth and Differentiation of Skin. (Last of three lectures.)

ROYAL SOCIETY OF MEDICINE
5 P.M *Section of Comparative Medicine* Mr T J Bosworth: Control of Livestock Diseases in Britain—Some Reflections on the Present Situation (Presidential address)
8 15 P.M *Section of General Practice* Dr F P Scott *Thirty Years in London General Practice (Valedictory address)*

INSTITUTE OF DERMATOLOGY
5 30 P.M Dr J O Oliver Disinfection and Sterilisation

Thursday 22nd

COLLEGE OF GENERAL PRACTITIONERS
6 45 P.M (14 Black Friars Lane E.C.4) Dr John H Hunt Present Position and Future of General Practice

BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M (London School of Hygiene and Tropical Medicine) Prof F G Young F.R.S Growth Hormone of Anterior Pituitary Gland

ROYAL SOCIETY OF MEDICINE
8 P.M *Section of Urology* Mr Hugh Donovan Malignant Cachexia. (Presidential address.)

INSTITUTE OF CARDIOLOGY National Heart Hospital Westmoreland Street, W 1
9 30 A.M Prof. M L. Rosenheim Œdema.

INSTITUTE OF CHILD HEALTH AND INSTITUTE OF NEUROLOGY
5 30 P.M (National Hospital Queen Square W C.1) Sir Russell Brain Paralyses of Cerebral Origin in Early Life Etiological Factors of "Acquired" Group (Virus Infections Lipoidosis Vascular Degenerative Diseases)

INSTITUTE OF DERMATOLOGY
5 30 P.M Dr R. W Riddell Structure and Classification of Pathogenic Fungi.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY 330 Gray's Inn Road W C 1
5 P.M Prof F C Ormerod Tuberculous Disease of the Upper Air Passages.

HARVEIAN SOCIETY OF LONDON 11 Chandos Street W 1
8 15 P.M. Dr Sheila Sherlock Jaundice (Buckston Browne essay)

UNIVERSITY OF DURHAM
4 30 P.M (Royal Victoria Infirmary Newcastle upon Tyne.) Sir Gordon Gordon Taylor: Rutherford Morison Tradition. (Rutherford Morison lecture)

MEDICAL SOCIETY FOR THE CARE OF THE ELDERLY
2 15 P.M (City Hospital Nottingham.) Opening of two-day meeting

HONYMAN GILLESPIE LECTURE
5 P.M (University New Buildings Teviot Place Edinburgh.) Prof. David Whitteridge F.R.S Cardiovascular Disturbances in Paraplegia.

Friday 23rd

ROYAL COLLEGE OF SURGEONS
3 45 P.M Dr G D Lumb, Irradiation Changes in Malignant Disease (Erasmus Wilson demonstration)

POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P.M Prof E. J Wayne Clinical Evaluation of New Drugs

ROYAL SOCIETY OF MEDICINE
8 P.M *Section of Obstetrics and Gynæcology* Mr Victor Lack Ectopic Memories. (Presidential address)

ROYAL EYE HOSPITAL
5.30 P.M. Dr A A. Guild Myopathies

INSTITUTE OF DERMATOLOGY
5.30 P.M Dr H J Wallace Clinical demonstration

INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
4 30 P.M (Queen Charlotte's Hospital, Goldhawk Road W 6) Mr A Bourne: Conservatism in Obstetrics.

LONDON ASSOCIATION OF THE MEDICAL WOMEN'S FEDERATION
8 30 P.M (Royal Free Hospital School of Medicine 8 Hunter Street Brunswick Square W C.1) Dr Lindsey Batten Scope and Limitations of Preventive Medicine

Appointments

ADAMSON W A D M.B. Edin., F.R.C.S.E consultant surgeon Royal Infirmary Edinburgh

FREEMAN A G M.A., M.D Camb., M.R.C.P senior registrar in *general medicine Exeter clinical area.*

LEES ROBERT, M.D Edin., F.R.C.P.E. physician (consultant) venereal diseases department, Royal Infirmary Edinburgh

SMITH A L G, M.B. Glasg., D.P.M deputy medical superintendent Cheadle Royal Hospital for Mental and Nervous Diseases Cheadle Cheshire

WADSWORTH W V., M.B , B.SC Manc., M.R.C.P D.P.M.: medical superintendent Cheadle Royal Hospital for Mental and Nervous Diseases Cheadle Cheshire

East Anglian Regional Hospital Board:

BIRNSTINGL, M. A M B Lond F.R.C.S. surgical registrar Norfolk and Norwich Hospital.

BROWNLIE J M., L.R.C.P E.: orthopædic registrar Norfolk and Norwich Hospital

CARTER, LEONARD M.B. Lond., M.R.C.P senior registrar in chest medicine Cambridge Chest Clinic

GUHA D D M.B. Calcutta surgical registrar West Norfolk and King's Lynn Hospital.

HOOPER E, R. S M B. Lond., D.A anæsthetic registrar Norfolk and Norwich Hospital

Amended notice

Notes and News

INVESTIGATIONS AT THE COLLEGE OF SURGEONS

ON Oct 7 the monthly dinner of the Royal College of Surgeons was followed by a demonstration of some of the work in progress at the college and at the Buckston Browne Research Farm at Downe in Kent

The respiratory and circulatory effects of reducing the body temperature of animals to various levels are being studied by H C Churchill Davidson, D Melrose, I K McMillan, and R Lynn, with a view to the safer use of hypothermia in surgery The blood flow in the limbs in poliomyelitis was demonstrated by A McPherson, and donor circulation experiments by A Andreasen In relation to the treatment of intestinal atresia in infants, H N Nixon is analysing the behaviour of the rabbit intestine joined by various types of anastomosis W J Dempster has continued his study of the homotransplanted kidney, and A E Kark was able to illustrate how, when the antrum is separated from the stomach and implanted in the colon, the flow of gastric juice from the remainder of the stomach can be grossly increased by stimulation of the separated antrum—e g, by its distension or by obstruction to the outflow of its contents B D Wyke, in a demonstration of cerebral localisation, was able to show, among other things, the increasing precision of methods of localising small lesions responsible for epileptic fits B E Greenfield displayed a portable electromyograph

The department of pathology had exhibits of heterologous transplantation of human tumours into mouse brain (George Lumb), the effect of androgen on hormone sensitive tumour (J Stretton-Young), cells in pleural and ascitic exudates (W Jayne), and changes in prostatic cancer after adrenalectomy (L Franks)

The demonstrations of the department of anatomy, by their diversity and close relation to function, bore witness once again to the change that has come over anatomy in the past twenty years—not least because of the collaboration of anatomists with surgical biologists such as V E Negus, who displayed the air conditioning mechanism of the nose D Tompsett showed the results of some elegant museum techniques, and Prof G Causey with H J Hoffmann showed a new model of electron microscope in action and some fascinating photographs obtained with it, using "ultra thin" sections (especially of nerves) prepared by methods which were also demonstrated Professor Causey and F Stansfield are examining the effect of vascularity on nerve grafting, and Simon Iversen is using a prototype interference microscope for the measurement of tissue density Miss J Dobson showed additions to the Hunterian Collection, Prof Kenelm Digby an experimental method of studying the ingestion of bacteria and dyes, and Professor Causey and R Sprinz a study of the effects of temporo mandibular meniscectomy

At the dinner Sir Cecil Wakeley, the president, drew attention to a portrait of Sir Henry Newland, of Adelaide, which has been brought to England by Mr A H Lendon and is to hang in the great hall when this is completed The portrait is a copy of one, by Andrew Meldrum, in the Royal Australasian College of Surgeons and was painted during his presidency of that college some ten years ago Sir Henry is shortly to hold his 80th birthday, said Mr Lendon, and one of his cherished memories is that he represented Australian surgeons at the centenary of the English college in 1900 and again at its 150th anniversary in 1950 Sir Cecil, describing Newland as one who has kept up with surgery in every part of the world, went on to speak with pleasure and pride of the decision of the American College of Surgeons to pay a visit to London "to see what we are doing"

THE MEDICAL SCHOOLS AND THE N.H S

THE aim of the undergraduate teacher, Mr IAIN MACLEOD lately affirmed, is to produce "an educated person grounded in principle and method, able to see what the whole of medicine stands for" Mr Macleod was speaking at the opening of the new session at King's College Hospital Medical School on Oct 2, and he went on to say that though as Minister of Health he was not concerned with the contents of the medical curriculum nor with the techniques of medical education, he was concerned with the end product, for he was by far the largest employer of those who emerged. Before 1948 most medical schools were under the ultimate control of the managing body of the hospital with which they were associated Today, he pointed out, medical schools were within the university sphere, and, in accordance sound principle, that the State does not university education, Exchequer assistance was the University Grants Committee, with whom the deal direct Many people felt—and he merely as a fact without coming down on either side— of the hospital service would be happier if to that method of financing the hospitals, by block grant, were instituted, and that was one he had asked Mr Guillebaud's committee to matter of urgency

SURGERIES AND WAITING ROOMS

UNDER his terms of service a general pract required to provide proper and sufficient surgery room accommodation for his patients, having regard circumstances of his practice" In a letter which been sent to every G P in the National Health Dr A Talbot Rogers, chairman of the general medical committee of the B M A, says that his committee every G P will do his utmost to provide the highest standard of surgery and waiting room accom Dr Talbot Rogers points out that recent question ment have made it clear that attention is likely to be upon isolated cases where the standard of su falls short of what is desirable, and the committee to forestall any criticism which might arise

The letter sets out the reasons which have committee to invite doctors to review the accom in their practice premises building restrictions less formidable, the widespread establishment of centres no longer seems likely in the immediate a result of the Danckwerts award, doctors may feel position to embark upon expenditure of this kind, practice expenses ratio established by the award substantial element in respect of the cost of surgery premises, so that a doctor who continues to premises of a substantially lower standard than the colleagues derives an unfair financial advantage

The committee thinks that it would be neither nor desirable to try to lay down any minimum it believes that any necessary improvements spontaneously from a wish by the doctors concerned that their premises are compatible with the of general practice in the National Health Service

DEVELOPMENTS IN RADIOTHERAPY

A NEW building which houses an 8 million vol accelerator and a 45 inch cyclotron has been the Medical Research Council at Hammersmith London. The central portion of the building is clinical rooms for patients and research laboratories

The linear accelerator, which is the first mach kind to be built for X ray therapy, has been de the Atomic Energy Research Establishment, the therapeutic Research Unit of the Medical Research and Metropolitan Vickers Electrical Company consists of a specially designed straight copper tube in length, along which a beam of electrons is acce very high frequency radio waves The electron be a gold target and X rays are produced These highly penetrating since they are generated by with an equivalent voltage of 8 million volts. In tional deep X ray therapy the voltage is 200 a few X ray therapy units in this country use 1 volts 2 million volts is also the effective voltage recently introduced cobalt 60 teletherapy unit The is positioned in the X ray beam by moving the treatment room up and down, and by using designed moving couch The three movements of beam, the floor, and the couch can be automatically by electronic equipment The high intensity of shortens the time of each treatment to about two and thus skin reactions do not develop Exten principles used in the 8 million volt linear accel made possible the design of a very compact machine suitable for use in routine radiotherapy ments, and the Ministry of Health has ordered machines for various hospitals

The 45 inch cyclotron is still under constru will produce an intense beam of high speed neu machine will be used for investigations into th *s on living and inert matter and an attempt will* le to determine whether neutrons are of value in the nt of malignant disease It will also be used for the ion of isotopes with a very short half life

NEW MEDICAL AUXILIARIES

Board of Registration of Medical Auxiliaries have ed the Association of Operating Theatre Technicians ognised qualifying body in medical auxiliary work Its is 23 Salmons Road Lower Edmonton, London N 9 ter of such technicians will be prepared and published course The association have recently inaugurated a urnal *Technic*, edited by Mr Eric Burton from St s Hospital, S W 1

TRIBUTE TO A PÆDIATRICIAN

Harold Waller has recently retired from the post of ician to the British Hospital for Mothers and Babies ich London S E 18, and a fund is being raised to morate his work since 1913 particularly on the problems ation on which his teaching has been adopted in ospitals both in this country and overseas Dr Waller g recognised that for some mothers a lying in period ays may be too short for the secure establishment of eeding and accommodation is needed at the hospital h a mother and her baby could return temporarily if ies arise. The purpose of the fund is to build a unit at the hospital where he worked for so many to accommodate one or two nursing mothers for short —not necessarily mothers with babies born at the l itself At least £2000 is required and contributions gratefully received if sent to the Dr Waller Fund at pital

THE W V.S IN ACTION

the sea broke through all along the East Coast on ht of Jan 31 this year from County Durham to Essex rs of the Women s Voluntary Services were among t on the scene—usually carrying urns of hot tea Nine later they are still on the scene helping people to their gardens ravaged by the flood waters. They have interval by feeding warming, clothing, and rehousing The report of their work (now published by Women s ary Services for Civil Defence 41 Tothill Street , S W 1) is brief modest and factual but the informal s that accompany it show clearly the kindness, resource and good humour that called forth the remark of lady at Lowestoft: I bin in three floods Miss, but he first one I've enjoyed

LAMBDA WAVES

a meeting of the Electroencephalographic Society 3 papers were read on the electro encephalogram early stages of sleep Dr W Cobb described a new nenon observed in the human electroretinogram under tensity flashes, and Dr M Roth gave further evidence existence of "lambda waves in the E.E.G., first ed by Dr C C Evans. These waves arise from random als occurring in the visual cortex and are often rved in E.E.G records owing to their low amplitude masking effect of background activity In 27 out of ects tested Dr Roth showed these waves in the ordinary They appear to be augmented by a short period of stimulation and are well brought out by scanning a ed or printed card The phenomenon is present anesthesia or normal sleep Summaries of the read can be obtained from the hon secretary Dr D A Maudsley Hospital S E.5

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rsity of St Andrews

graduation ceremonial on Oct 9 the degree of doctor of ne (with commendation) was conferred on J le

National School of Medicine

C W D Lewis, who is at present lecturer in surgery n appointed senior lecturer in surgery at the school

College of Physicians of London

E. J Wayne will deliver the Bradshaw lecture on lay Nov 12, at the college, Pall Mall East S W 1 speak on the Diagnosis of Thyrotoxicosis On Nov 19 ffor Evans D LITT will deliver the Lloyd Roberts on Science and Literature Both lectures are at 5 P M

Royal College of Surgeons of England

At the meeting of the council on Oct 8 with Sir Cecil Wakeley president in the chair Sir James Learmonth was appointed the Sir Arthur Sims Commonwealth travelling professor for 1954 It was reported that Sir Cecil Wakeley had been appointed the Hunterian orator for 1955

Dr E Rohan Williams was admitted as the coöpted member of the council representing radiology Mr J H Doggart Mr R J Cann and Mr A. H Lendon were admitted to the court of examiners

The Ophthalmological Research Unit which has been in existence for ten years under the direction of Prof Arnold Sorsby was admitted to the status of a department of the college

The Sir Gilbert Blane Naval medal was presented to *Surgeon Captain J G Holmes* *Dr R Wyburn Mason* was awarded a Prophit research studentship The Handcock prize was presented to Mr J J Jones Mr C Ross was admitted as a Macloghlin scholar

The council approved the institution of a Mitchiner medal to be awarded annually in memory of the late Major-General Philip Mitchiner for outstanding services to military medicine by an officer of the Army Medical Service or R A.M C A similar medal presented by Sir Stanford Cade for award to a medical officer of the Royal Air Force was instituted in memory of the late Lady Cade

Diplomas of membership were granted to F J Morley and S. C C Scott The following diplomas were granted jointly with the Royal College of Physicians, to the following candidates

D T M & H—Ainuddin Ahmad Fatima S Ahmed J A S Amos, R. P Bradshaw T M W D Arcy M W Dhurandhar J M Dube J R. Eloy J I T Glover G H V Keshani H D Madsen T C/H Mathews Roger Mortimer Shankar Rao Guillermo Angel Leal Shafiqur Rehman A D Roe J G Slater Majuree Sundaravej S G Talpade Margrit Zuber

D C H—O. A L Abrams, Ainuddin Ahmad R N Akel, Anthony Allibone Kooki N Bharucha, H C H Bird Irene F A Blakeney Michael Brando Neville Broughton Dorothy F M Burnett Joan M. Cashman, Margaret J Cox Marion E Cox Diana F J Duncan, O. N Faith Eva O Faulkner Carol A Foxell Margaret J Francis Jessie S Freeman A K Ghosh J C Gillespie Bandana Gupta, D T G Harris W B McN Howie Jasmine R Jacob, Basil Jaffe F E James K V Jones Winifred A Kane A J Keay P J, E. Lewis Joo Leo Lim Daphn H Line A D Macdonald K. W Matheson Joan M Mawer Margaret B Mearn J L. Miller B J L. Mies, J W Muller C W A Murray Gwendoline D Newman M N Orton Varadarajan Pillai, Dafor E MacG Plowman Theresa Posner O C Raffel, Myrtle J Raynor Ellen L. M Rhodes Nancy M E. Robertshaw Hilary O Rubin David Satya Nand M K. Sawday D H Shennan, Priyani E Soysa Sara I Stinson T E. Stockley Elsie O Taylor Katharine J Thicknesse A J Thomas Elizabeth S Tomlinson Pamela S Triplett Joan E. Walton Sheila M Watts Johannes Wessels Enid M Whitfield, T K Williams Irena H Wittek

D A—J Q. Richardson.
D I H—K B Roy
D L.O—J B Blacklay
D O—R. Smith

Faculty of Dental Surgery—At a meeting on Oct 9 the Board of Faculty of Dental Surgery elected Prof F C Wilkinson dean and Prof H H Stones vice dean for the ensuing year

Royal Faculty of Physicians and Surgeons of Glasgow

At a meeting on Oct 5 with Dr Andrew Allison the president in the chair Tavi Anjaneyulu Naidu was admitted a fellow of faculty *qua* physician.

Ciba Foundation

Prof A von Muralt (University of Berne) will deliver a foundation lecture on Thursday Oct 29 at 1 Wimpole Street London W 1 at 5 P.M He will speak on Neuro physiology—Old and New Facts and Theories

Immunisation in Young Children

A conference on this subject will be held at the Highgate wing of Whittington Hospital Dartmouth Park Hill London N 19 on Saturday Oct 31 at 2.30 P M Papers will be read by Dr W C Cockburn Dr S King and Dr T M Pollock Tickets may be had from the pediatric department of the hospital

King s College Hospital Dinner

The annual dinner of King s College Hospital Medical School held in London on Oct 3 with Mr V E. Negus in the chair was attended by 145 past and present students and guests Mr W I Daggett proposed The Chairman, and Mr Negus proposed The Medical School. On this domestic occasion their speeches were informal but gave none th less pleasure

International Congress of Industrial Medicine

This will be held at Naples from Sept 13 to 19, 1954 The hon secretary of the British members is Dr P Pringle, British Electricity House, Winsley Street, London, W 1

West London Medico-Chirurgical Society

At a meeting to be held at the South Kensington Hotel, 41, Queen's Gate Terrace, S W 7, at 8 30 P M, on Thursday, Oct 29, Mr C Hamblen Thomas will deliver a presidential address entitled Featuring the Nose

Society of Public Analysts and other Analytical Chemists

A meeting of this society will be held at 5 P M on Oct 23, at Southampton University, when Mr F H Pollard, PH D, Mr Roy Markham, PH D and Dr A L Latner will speak on Paper Electrophoresis

University College Hospital

The annual dinner of past and present students of the medical school, will be held at the Savoy Hotel, Strand, London, W C 2, on Friday, Oct 30, at 8 P M Dr Kenneth Stokes will be in the chair Tickets (£1 7*s* 6*d*) may be had from the dinner secretary, University College Hospital Medical School, University Street, W C 1

British Occupational Hygiene Society

The first conference of this society will be held on Monday, Nov 2, at 11 A.M, at the London School of Hygiene and Tropical Medicine, Keppel Street, W C 1 The conference, which is open to non members of the society, is designed to provide a common forum for the many professions—medical and non medical—concerned with occupational hygiene Further particulars may be had from Mr P C G Isaac, the hon secretary of the society, Public Health Engineering Laboratory, King's College, Newcastle upon Tyne

London Hospital Dinner

Mr George Neligan, presiding at the old students dinner on Oct 8, began by speaking of former members of the staff who had died during the year, A B Roxburgh, R J Probyn Williams, Charles Goulden, and G E Vilvandré He welcomed as new members Dr J S Pegum (dermatology) and Dr S L Last (electro-encephalography) By retirement the hospital had lost Dr W J O'Donovan ("who has cured your scabies for so many years") and the medical college its dean, Dr A E Clark Kennedy As dean for 18 years, and previously as subdean for 5 or 6, Clark Kennedy had "done his damnedest" and had shown himself always a real Londoner happily he was remaining at the hospital disguised as a physician Though the college and hospital now had separate charters and the college belonged to the university, their separation was merely on paper they worked together just as before Dr Clark Kennedy, responding, said that any limited success he had achieved in the medical college was due, first, to having a permanent alibi ("when asked to do anything in London I have had too much to do in Cambridge" and vice versa), and secondly to having people to do all his work for him He had been lucky in inheriting Mr E J Burden and the late H A Osman, and wise in choosing Mr H P Laird as secretary and Dr John Ellis as subdean The college had been most fortunate in its friends, "and in memory one among them will always outstand—our chairman" Three unsolved problems he must hand to his successor First, the medical college had grown, like other institutions, a bit too big, secondly, in view of the changing nature of the hospital's clinical material it might have to use other hospitals for teaching, and, thirdly, he was convinced that the student ought to be introduced to clinical medicine much earlier in his training Dr A G Maitland-Jones, proposing The Chairman, claimed to have seen more of him than any living man for he had assisted the late James Sherren to perform a laparotomy upon him —and those who remembered the extent of the late James Sherren's incisions would agree The London Hospital and its students had never had a better friend than George Neligan His generosity in time and money had never been equalled, and he had played a big part in carrying the hospital through the war In 41 years of friendship Dr Maitland-Jones had yet to hear him say an ill word of any man in all these years his attitude had been "with malice toward none and charity toward all"

Those who attended the dinner will long remember the ovation given to their chairman when he first rose to speak

London Medical Exhibition

Lord Horder is to open this exhibition at 11.3 Monday, Nov 16 The exhibition, in the new Royal Horticultural Society, Greycoat Street, continue until Nov 20, opening on the last 11 A M and remaining open each day until 6.30 P.M.

Competition for Medical Films

The *Presse Médicale* is again offering a prize francs and other awards for the best medical films submitted by amateurs

The films (16 mm) may not be subsidised by a laboratory or firm Further particulars may be had secretariat of the journal, 120, Boulevard Saint-Films should reach the secretariat not later than March

Nuffield Inquiry into the Causes of Crime

The Nuffield Foundation has invited Lord undertake a critical appraisal of current views—by actions and in writings—of the causes of crime. be assisted by a small group of assessors, Dr Desmond Curran, psychiatrist to St George's Hosp Dr T C N Gibbens, lecturer in forensic psych Institute of Psychiatry in the University of London

Medical Statistics

The study circle on medical statistics of the Royal Society will meet on Tuesday, Oct 27, at 6 P.M. at minster Medical School, Horseferry Road, London, report on Measures of Morbidity in Public Heal Statistical Aspects of Disease Classification F lars may be had from Mr M P Curwen, St. Barth Hospital, E C 1

British Postgraduate Travelling Fellowships

The British Postgraduate Medical Federation applications from doctors and dentists for these fe which have been set up to enable graduates who are as specialists in one of the preclinical or clinical medicine, surgery, or dentistry, to obtain experi methods of practice, education, and research at or other centres in the United Kingdom and abroad. particulars will be found in our advertisement columns

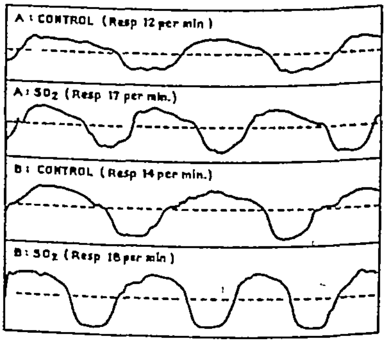
Synthesis of Oxytocin

Prof Vincent du Vigneaud, who holds the chair chemistry at Cornell University Medical College, is reported to have announced in the *Journal of the Chemical Society* the synthesis by himself and his of oxytocin (*New York Times*, Oct 7) The same the society's journal contains an article from Vigneaud's department giving a proposed chemical for vasopressin

Society of Chemical Industry

This society's food group (nutrition panel) is to series of meetings with the general title Reappraisals At the first meeting, to be held in of the Chemical Society, Burlington House, London, W 1, on Wednesday, Oct 28, at 6 30 P.M., Bender, PH D, will speak on Proteins Later meet deal with Calories and Basal Metabolism (Dec. 9) and (Jan 27)

CORRIGENDUM *Effects of Inhalation of Sulphur Man.*—In the by Dr An her colle week (p. base line omitted fr tracings in The accom figure sho tracing w base-lines The area curves, re in the seco graph on the area e the curve base line



CHILDREN IN HOSPITAL

PREPARATION FOR OPERATION

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DREN'S reactions to operations vary Many
lly if over five years old seem quickly to forget the
hospital and its necessary unpleasantnesses A
m to behave better afterwards, as if surviving an
nce they thought would be bad has given them
onfidence in life and in themselves. A considerable
r, chiefly among those under five show changes in
our for a shorter or longer period after The
s are chiefly fears—of the dark of being alone in
ratory, *of being alone—and regression to more*
behaviour such as wetting by day or night
g to be fed or negativism Fears of doctors,
and strange men are frequent fear of the dark
fear of separation from the mother which may
ow itself as insomnia In some children a later
hospital or doctor reveals fears that were not
at home

tivistic reactions—disobedience, tantrums spiteful
fiant behaviour—occur chiefly in children of five
r older and can greatly try parents on the child's
home Increased dependency is another symptom
n be wearing to a busy mother It is so common
e almost a normal sequel.

nan (1949) regards psychological trauma after
ctomy as a *complication as deserving of the*
s thought as is postoperative bleeding or infection
aration is often the occasion of a child's first
ion from home, or if he has been away before it
a happy visit without attendant anxiety It is
for people who work in a hospital to appreciate
iety that the special event of going into hospital
for any but the most self-confident. Strange
trange food, a strange routine an unfamiliar bed—
e ceiling is unusually distant Langford (1937)
g 20 children with anxiety states found that in 6
rder was related to tonsillectomy for which the
had, as a rule been poorly prepared Of another
f 124 children who had had operations often a
ctomy 25 had emotional upsets for longer or
time (Levy 1945) The symptoms were most
n at the ages of one and two probably because the
were then more dependent on their mothers did
derstand what was happening and could not get
heir anxiety in words or play Night terrors were
en in these younger children for months.

evy's series, in 13 of the 25 children who were
othing beforehand had suggested that this would
It is *true that a child who* has shown lack of
fidence is more likely to be upset but one cannot
that a happy confident child of two three, or
ll necessarily show no disturbances Sometimes
first operation has produced little disturbance a
will disclose that the first left after effects.

hildren who come into hospital for operations
nce some degree of anxiety The film *A Two*
Goes to Hospital (Robertson 1952) *shows clearly*
happy self-controlled little girl reacted She
at her lips clung to her doll was unusually quiet
e minutes to thaw when her mother visited her
on This film opens one's eyes to the quiet
iness that a young child in hospital may suffer
f the day almost unnoticed by the nurses and
We do not want to see the grief and we see
good quiet child If a child is crying we may
this crying to the crying of a small child who is
hungry or has fallen We tend to dismiss all crying as common and unimportant

Three Anxieties

The three main anxieties which centre round an admission to hospital for operation are the separation from home the anæsthesia, and the operation.

SEPARATION

Some children under four feel so lonely and deserted that they do not seem to notice the operation much This is especially true of children who have to stay longer than they expected and of children who are not too trusting of their parents statements (Jessner and Kaplan 1949) Older children can understand the separation as an episode the younger child has a more intense attachment to his mother and may react severely, *and even if he settles down he may reveal that he felt* intensely by his behaviour on returning home Bowlby (1951) has shown that mental health and ability to get on with people in later life may depend on a warm and continuous relationship with a mother (or permanent mother-substitute) Severe deprivation can seriously disturb personality It seems probable that shorter deprivations may lead to slighter but still handicapping disorders such as diminished self-confidence Even if it did not sadness in small children is something to be avoided as far as is in our power The child reasons and if he is anxious he may conclude that his mother left him because she did not love him To an anxious person in a strange world the most fantastic idea may seem reality

ANÆSTHESIA

The fear of losing control as they feel themselves slipping away under the anæsthetic is common in older children (of say six to twelve years) given ether for tonsillectomy (Jessner and Kaplan 1949) Children sometimes have unexpressed foolish fears of what will be done while they are under the anæsthetic sometimes from what thoughtless children or grown ups have said A kindly nurse said what lovely eyes you have I wish you'd let them change them for mine while you're under the ether Some small children genuinely fear they may die a little girl's first statement on coming round was: I didn't die

OPERATION

Children's ideas about operations and even about minor incidents of hospital routine, can be surprising Some children will say they want their tonsils done so that they can have ice-cream like their brother had after tonsillectomy Some imagine they are to have major procedures that have happened to their parents—thyroidectomy gastrectomy—details of which have been overheard at home

Sometimes needles rectal temperature-taking hospital clothes, or being put into a cot are disturbing children sometimes interpret them as punishments for real or imagined naughtiness

Some have remarkable fantasies as to what happens in so-called minor operations The child newly admitted for tonsillectomy may silently assume that this is what has been done to the child in the next bed with his eyes *bandaged Incidentally quite a few children wonder* what becomes of the appendix or tonsils removed and rather resent that they are thrown away as rubbish

According to Jessner and Kaplan (1949) the children who cope best with hospitalisation are the confident children who can transfer positive affection from the mother to the nurse those who interact with other children those who are interested in games and toys those who can express themselves *indirectly* by crying anger or naughtiness, with only moderate limitation or self control "The child should be given the opportunity to express as much of his feelings as his own standards allow him to One should not interfere with this capacity for self-expression by an effort to coach the child to be good and brave"

It seems important to let the child set his own standard of self-control, reassuring him where possible about his fears but accepting these and his tears with sympathy, remembering the therapeutic benefit of a good cry for grief-stricken adults, and remembering also that a temper tantrum is itself a frightening experience for a child, for which he needs to be comforted

Some children behave better and are happier after operation because their health is better Among older ones, a few may be better for the emotional experience Most normal children and some "insecure" children escape lasting emotional sequels Many more or less disturbed children and some normal children show evidence of anxiety after operations (Levy 1945) Some children who seem to take the experience very easily, show by behaviour long afterwards that they have suffered, asthma may date from an operation such as tonsillectomy

How the Doctor Can Help

Can I see another's woe
And not be in sorrow too ?
Can I see another's grief
And not seek for kind relief ?
Blake. Songs of Innocence.

What can we do about these possible effects and after effects of a stay in hospital ? Coleman (1949) suggests the following helpful measures

1 Give the child a forthright and honest explanation of the reasons for the operation

2 Try to avoid the element of surprise and confusion at the hospital A recognisable picture of the hospital, the operating-room, and the white-gowned nurses and doctors should be presented in advance

3 Explain that the purpose of anæsthesia is to spare the child pain during the operation. Assurance must be given that this forced sleep is temporary and will be followed by complete awakening and survival The ideal anæsthetic is one chosen for surgical efficiency and psychic consideration

4 Emphasise to the parents the need for constant reassurance and affection in the postoperative period

5 Whenever possible, the doctor personally should lead the child from the mother to the operating-room The previously established child-doctor rapport here pays dividends in the sustained security

6 Permit overt expression of postoperative hostility, rather than suppress it The psychic damage of such suppressions is fraught with subsequent danger

Levy (1945) and Jessner and Kaplan (1949) suggest postponing operations, if possible, until the child is at least four, when it is less disturbing for him to be separated from his mother and when he can understand something of the meaning of the operation The disturbance is perhaps least between the ages of five and ten years Operations should also be postponed if possible in children who are unusually timorous or dependent on their mothers If operation is unavoidable special care should be taken before, during, and after hospitalisation Operations are also best avoided at a short interval after a previous stay in hospital or other separation, after a family bereavement, or when the mother is having another baby, or even while the family is moving house

BEFORE THE OPERATION

It is clear from *A Two-year old Goes to Hospital* that a familiar toy, slippers, clothes, or other tangible tie with home can be a reassuring comfort Parents should not be to let the child bring the favourite shabby doll or toy In this film a doll and a very shabby blanket were wisely allowed to the child with about sepsis after all virulent germs are rare in households

> "One youngster in the Harriet Lane Home (the hospital at Johns Hopkins Hospital) had a pair of which he insisted on wearing in bed. They stay in bed for several days except when he allowed th take them off He wore them up to the operating only permitted them to be taken off after arrival (Trainham 1949)

The parent should indeed be specifically bring some such toy The familiar object a child because he knows himself as the owner object—and there it is beside him in his similar reasons the child should come back theatre to the same bed in the same room before, otherwise he may worry that his know where he is

In running the ward, discipline and routine adapted to the individual child's need. T punishments are out of place and a period in rarely the right time to teach better manners or to cure children of sucking their thumbs or dummies

A preoperative sedative is nearly always although some children become excited and The anæsthetist does a great deal to allay a child's especially if he knows what these fears are McDonald (1953) has described the usefulness sodium thiopentone in lessening postoperative disturbances in children

Twenty-four hours in hospital before a child to get over his first panic and to establish with his fellow patients, the nurses, and doctors. tedly this lengthens the period of separation, have recommended that operations on young should be done in the home But the possibility operative complications is a potent argument this "The solution is to bring the home hospital" (Foord, 1949)

The doctor who admits the child to hospital mindful of childhood's problems The pædiatric officer often appreciates these better than his colleague who has had no special experience in and may forget to explain things to mother and

The Mother in Hospital

The mother brings the child to hospital and hospitals gives him his bath and puts him in it is certainly possible for her to be there while gives him his bath if he is dirty she may learn standards of cleanliness Even the examination lice need not be postponed till the mother is mothers of children at local authority schools to their children's heads being inspected. bath the mother explains things to the child having told him when she will be back again, going away and goodbye With babies, not, it is ideal for the mother to come in with In New Zealand the Pickerills, for their operations, have a hospital built on the chalet principle for mothers to come in with and their babies

Daily visiting is always wise and humane If is anxious, she should be reassured by Mothers can be led to understand how their adversely affect their children In an air raid mother with her child in her arms was shelter when she realised her terror was felt child She slowed to a walk, looking up and out the "lovely aeroplanes" droning above

Sometimes parents are distressed because their cry or turn away when they come to see them.

that a child may remember in a rush how much he)een missing Anna Freud has said it is important ll children in hospital three things :

He is still very much loved
He is not being punished
He is getting better

nurses and mothers should put these things into)s to all children, however small and however happy seem It can do no harm and may give great relief ors, nurses, and parents all do well to give a child, ver small, credit for understanding—or feeling— i is said or felt.

hen it is suggested that mothers should come into ital with their children it is usually pointed out they may be *anxious and upset the child* Mothers and this would be true of some of them ; but the nent is sometimes a rationalisation of a desire to the mother out of the way This is not always ntirely unreasonable attitude for the confident ude of the regular nursing staff is helpful to a

has been suggested that mothers should accompany ren to the induction, but it may be upsetting to a to find that his mother coöperates in the " attack im. If a preoperative sedative is given it seems cessary for the mother to go to induction of a semi ious child When a child does not have a pre itive sedative, he should be carried to the anæsthetic by a familiar nurse or accompanied by the nurse porter carries him and that this nurse should stay him until he is unconscious Certainly being lled on a trolley lying flat so that one cannot see e one is going is alarming The first waking of a after operation would alarm some mothers, and child probably would not realise whether she was or not. The mother should, however visit on the ing of the day of operation The ward sister should her if the child is likely to be confused or bloody ough children in hospital are more difficult when their iers are admitted with them, the postoperative ulties are so much less that Escalona (1949) agrees it is worth while

iother suggestion for bringing the home into the ital" is to allow children to eat home-cooked food iout experience it is difficult to say whether this d be worth arranging but food prepared by his ier might mean a great deal to the child apart from 'act that children are conservative and like the sort od they are used to Some children comfort them in hospital by eating more than they do at home n a child s mind food and his mother are closely lated.

Telling the Child

ie parents have an extremely important part to in preparing the child before he goes into hospital. important that they and he both know what will en there The mother and father must know what happen in hospital so that they can answer the tions the child is certain to ask. It is a good plan he child to enact at home the admission to hospital anæsthesia, and the operation

hildren will also be helped if they know beforehand they are likely to miss their parents and may be ly A mother of two children, aged 8 and 10 years divorcing her husband. She explained the situation he little girls who remained with her throughout er the 10 year old said Mummy you told us what ld happen, but you didn t tell us how we d feel ' idred 1953) Edelston (1943) has remarked that clinical experience the determining factor (for ptoms after separation) seems to be the degree of ction or insecurity *felt by the child* "

How long beforehand should the child be told ? Some say months, some say a few days It probably should be shorter for the more timorous children Certainly the child should be told so that what happens is not all unexpected.

The parents and everyone else concerned should also know what *not* to tell children A medical student tells a child about to have a laparotomy that ' it won't hurt." Yet the child's abdomen *will* hurt after the operation A mother, as she leaves tells her child that she will be back in a minute " Another tells her child that she will be sleeping in the room below (so the poor child later went on to the balcony and screamed ' Mummy Mummy ') A little girl is told to behave—or she will be left in hospital ' an anxious boy about to go into hospital is told to stop playing with himself or the doctor will cut it off while you are under the anæsthetic "

These remarks are not made in malice even though they are untrue and wrong The parent says Oh he is too young to understand,' which is almost certainly not true or I didn t want to make him unhappy,' although in the long run the discovery of deceit is more upsetting Undermining the child's confidence in what he is told does not help the hospital staff and often a child can accept unpleasant news more easily from a parent It is fairly easy to understand a medical student with no experience of bringing up children comforting a child by misleading statements it is less easy to under stand parents doing this. Telling such palpable untruths does not make bringing up children easier and apart from that it is a poor example Anyway telling the truth is an important principle of science in general It might " ring the bells of heaven ' quite loudly if we stopped telling children this won t hurt you just before sticking a needle into them

Parents, and especially the mothers need guidance in preparing a child for the experience of being in hospital It might be useful to prepare a leaflet for them to read One thing is certain adults deceive themselves when they dismiss the facts that small children in hospital are often anxious or sad, and that such anxiety often permanently lessens the child s reserves of self-confidence They are in fact, resorting to a functional blindness by which *they spare themselves awareness of children s* suffering

This article arose from a conversation with Miss Tanner sister of the children s surgical ward at Guy s Hospital and I thank her Miss Duncombe of the children s medical ward Mrs. M Oppé and Dr P E Polani Dr D G Vulliamy Dr T E. Oppé Dr P J Lyne and Dr D M E. Allen of the department of child health, Guy s Hospital for their help

The influence of Dr H C. Cameron s example of under standing and sympathy with children will be evident and it is appropriate that Guy s was the first teaching hospital in London to have regular daily visiting of children

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RADIOGRAPHY IN THE DIAGNOSIS OF HYALINE MEMBRANE

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With illustrations on plate

THE diagnosis of hyaline membrane within the lungs of infants dying in the first few days of life can only be made with certainty post mortem The association of this membrane with atelectasis is now increasingly recognised , and, since atelectasis is generally accepted as the most important single cause of death in premature infants, the clinical importance of being able to diagnose hyaline membrane during life is obvious

Claireaux (1953), in his histological examination of the lungs in 376 cases of neonatal death, found hyaline membrane in 108 (29%), of which four fifths were in premature infants and in no less than 21% of the 376 cases hyaline membrane was the only abnormality discovered

Unfortunately it is no easy matter to diagnose the cause of a baby's respiratory difficulties on clinical grounds alone At best a shrewd guess may be made that hyaline membrane may be present if a baby, within the first few hours of life, exhibits increasing dyspnœa, grunting respirations, inspiratory recession (either subcostal, intercostal, sternal, or suprasternal), the use of accessory muscles, cyanosis, poor air entry, and bouts of apnœa The diagnosis is still more likely if the baby is premature or has been delivered by cæsarean section because of maternal diabetes , but a similar clinical picture can be evoked by other conditions such as intraventricular and subdural hæmorrhage, primary atelectasis, pneumonia, œsophagotracheal fistula, diaphragmatic hernia, and pulmonary hypoplasia The ante-mortem diagnosis of hyaline membrane might be of little more than academic interest were it not for the possibility of treatment and the bad prognosis which these clinical signs often betoken

To learn how far this pathological process is reversible demands an ability to diagnose it before death, and the success of any treatment adopted can hardly be substantiated without the diagnosis, except perhaps on the quicksands of statistics, if the infants recover and do not come to necropsy

In our researches into neonatal atelectasis and its treatment it is therefore natural that we should have invoked the help of radiology

The extent to which babies in respiratory distress are not radiographed is common experience, and is possibly part of the traditional " no touch " technique Nevertheless, both in diagnosis and in assessing progress, we have found radiological investigation of considerable help when taken in conjunction with clinical examination, spirometry, and other diagnostic aids

Surprisingly little has been published in this respect Caffey (1945) noted radiological signs in the lungs of premature infants but dismissed their pathological significance An article by Donald and Lord (1953) on augmented respiration in the treatment of neonatal atelectasis was illustrated by radiographs showing radiological signs in some of their cases in which hyaline membrane was found at necropsy Two months later Meschan et al (1953) published a case of proved hyaline membrane and demonstrated radiological changes which are now familiar, but we have been unable to find a sequence of radiographs comparable to those we now reproduce

Three different stages in the evolution of membrane have been identified radiologic correlated with the clinical and necropsy findings

(1) First there appears a fine miliary mottling th the lung fields

(2) This is followed in the progressive lesion by and more coalescent type of opacity At this st bronchial tree is often clearly demarcated

(3) Finally the shadows become confluent as a lobar or lobular consolidation and collapse

The baby may die of some other lesion—e.g., an intraventricular hæmorrhage—before all three are radiologically demonstrable and unless radi are taken every few hours it is likely that the of events will not be observed

Up to date 28 newborn infants at Ham Hospital with respiratory distress have provided of radiological interest which are here described. other cases so investigated do not concern the of this paper and have been omitted The cas been divided into five groups as follows

Group I —Significant radiological signs, and membrane found at necropsy (11 cases)

Group II —Clinical signs of atelectasis, but no radi signs, and hyaline membrane not found at necropsy (

Group III —No radiological signs, but hyaline me found at necropsy (0 cases)

Group IV —Radiological and clinical signs pres child recovered , diagnosis therefore unproven (4 cas

Group V —Radiological signs present, but lesions than hyaline membrane at necropsy (5 cases)

The last group might be called the false positives

Case-records

GROUP I

(Radiological Signs Confirmed at Necrop

Case 1 —One of twins, the other being anen delivered at 32 weeks Birth weight 3 lb 8 oz. Cy grunting, and clinical signs of atelectasis at 1 hour mented respiration produced temporary improvement Died at $9^3/_4$ hours

Radiography at 3 hours showed fine mottling but n collapse (fig 1) At 8 hours radiography showed mottling, the degree of collapse was progressive and the lower lobe appeared solid (fig 2) At necropsy there almost no aerated areas of lung, and microscopy hyaline membrane Death was attributed to atelectas intraventricular hæmorrhage was a contributory facto

Case 2 —Lower segment cæsarean section at ter antepartum hæmorrhage Birth weight 6 lb 8 oz Ha well for seven hours, when cyanosis occurred and s atelectasis rapidly developed She was intubated at $9^1/_2$ and oxygen was supplied with intermittent positive Respirations were augmented from 11 hours with improvement, the endotracheal tube remaining in s for technical reasons the treatment was discontinued 6 hours and the child died at $17^1/_2$ hours.

At $9^1/_2$ hours radiography showed coarse mottlin post mortem it showed total collapse At necropsy o anterior border of the right upper lobe floated, a presence of hyaline membrane was confirmed histolo Death was attributed to secondary atelectasis

This case has previously been described with illustrations (Donald and Lord 1953, case D1)

Case 3 —Delivered at 33 weeks Birth weight 4 lb Cried at once, but respirations became irregular with and inspiratory recession Died at 7 hours. At death was attributed to atelectasis. A subdural on the right was regarded as a contributory factor pulmonary aeration was macroscopically visible, a microscopy the alveolar ducts and respiratory bron were seen to be overdistended and lined with hyaline brane The radiograph before death showed co shadows in peripheral lung fields, with sharply o bronchial tree (fig 3), and post mortem almost deflation (fig 4) in spite of attempts to reinflate after the absence of earlier films it might be difficult 3 to distinguish between primary atelectasis and ced hyaline membrane on radiological evidence , but the prominent bronchial tree is significant may suggest hyaline membrane with peripheral tasis.

se 4—Delivered at 28 weeks. Birth weight 2 lb 1 oz. netry at 2 hours showed a minute volume of 410 ml respiration. Radiography at 11 hours showed incomplete on and death occurred at 12 hours At necropsy a intraventricular hæmorrhage was found responsible for but the lungs showed only patchy aeration of the portions of both upper lobes and the right middle lobe atter alone floated Histologically many respiratory hioles and alveolar ducts were overdistended and lined aline membrane The surrounding lung was collapsed *were also signs of early pneumonia*

out the earlier spirometric record one might have in doubt whether the radiological signs were those imary atelectasis or hyaline membrane

se 5—Alleged gestation 28 weeks, probably 32 weeks. weight 4 lb 2 oz. There was sternal recession, cyanosis, grunting His condition steadily deteriorated and at the f $4^{1}/_{2}$ hours respiration was augmented, with improvein minute volume but seal leaks developed at 9 hours at $10^{1}/_{2}$ hours

diography shortly after admission at $2^{1}/_{4}$ hours showed tippling throughout the lung fields with clear definition bronchial tree and a further film at 10 hours showed ation and coarser and increased mottling At necropsy the infero anterior border of the right middle lobe was aerated, and the presence of hyaline membrane was med on microscopy Death was attributed to secondary tasis.

se 6—*Breech delivery at 26 weeks following ante*m hæmorrhage Birth weight 2 lb 8 oz. There was unced recession and grunting Became moribund at 5 and died at 8 hours. Radiography at 5 hours showed it no evidence of pulmonary inflation but the bronchial was well outlined

he absence of earlier radiography it would be ult to distinguish the radiological appearances those of primary atelectasis, apart from the possible ficance of the demarcation of the bronchial tree ecropsy death was attributed to atelectasis there little evidence of aeration, and microscopy showed ine membrane

se 7—The third of triplets delivered at the 33rd week, nother having pre-eclamptic toxæmia. Birth weight 16 oz. Initial condition good, but grunting respiration vened, with severe recession. At 7 hours respiration ugmented until technical troubles developed after three . Recession persisted, and death took place at 20 hours. diography at 6 hours and 12 hours showed coarse ling, which in the later radiograph had become more ounced The bronchial tree was well demarcated At psy both lungs were unaerated and microscopy showed sive hyaline membrane Death was attributed to ctasis.

se 8—Delivered at 34 weeks. Birth weight 4 lb 6 oz. l well at birth but became cyanosed Subcostal recession conspicuous within ten minutes. Respirations were ting Inspiration was augmented intermittently with ive pressures from the age of 35 minutes onwards with temporary improvement Repeated cyanosis was *wed by death at 9 hours.*

diography at $3^{1}/_{2}$ hours and half an hour before death ed bilateral atelectasis involving segments of upper and r lobes. The bronchial tree was well outlined and the ad radiograph showed little improvement At necropsy was only patchy aeration of the right lung (positive ure insufflation had been continued post mortem) oscopy revealed hyaline membrane Death was attributed telectasis although there was also a small intraventricular orrhage

se 9—Precipitate delivery at 29 weeks after painless partum hæmorrhage Birth weight 3 lb 13 oz Severe yxia at birth with much inspiratory recession Condition rapidly deteriorated, gastric oxygen was administered but the heart stopped after two hours. Radiography immediately after death showed total collapse of both lungs, without any evidence of aeration (fig 5) Necropsy showed gross atelectasis and on section the lungs were *found to be slightly expanded* as a result of aspiration of liquor amnii Some of the alveolar ducts showed developing hyaline membrane

This radiograph differs from that of the previous case particularly in the absence of demarcation of the bronchial tree and we are inclined to regard this picture as essentially one of primary atelectasis although hyaline membrane was found

Case 10—One of twins. Breech delivery at 27 weeks. Birth weight 2 lb 2 oz. Considerable recession, mainly subcostal, and respiration was augmented Repeated cyanosis ensued and was followed by death at $38^{1}/_{2}$ hours.

Radiography at $2^{1}/_{2}$ hours 14 hours and 10 hours showed granularity and outlining of the bronchial tree At necropsy the right lung floated as a whole but only the middle lobe was reasonably well aerated Both lobes of the left lung sank, and only the anterior border and lower tip were aerated There was a large bilateral intraventricular hæmorrhage and clot was present *in the fourth ventricle* Death was attributed to this, but the lungs on section revealed early hyaline membrane as well constituting a contributory factor

The other twin (mentioned elsewhere) showed radiologically good expansion and no hyaline membrane was found post mortem It too died of intraventricular hæmorrhage It appears that the finer the granularity the earlier is the stage of development of hyaline membrane

Case 11—Delivered at 35 weeks. Birth weight 3 lb 3 oz Baby was admitted at the age of 6 hours with pronounced inspiratory recession and grunting respiration. Condition at birth initially good During the first 30 hours respirations were intermittently augmented with temporary improvement in the child's colour but recession persisted Jaundice developed at 62 hours with hardening of the skin Death took place at 68 hours.

Radiography at 8 hours (fig 6) 11 hours 26 hours about 30 hours (fig 7) and 48 hours (fig 8) showed very fine mottling throughout both lungs with partial deflation on the left which progressed in subsequent films, but in the 48-hour film some re-expansion of the left lung had taken place and the mottling throughout had decreased, suggesting regression in the alveolar deflation At necropsy the left lung sank the right lung floated and showed partial aeration, and microscopy showed extensive hyaline membrane vascular congestion and some intrapulmonary hæmorrhage Death was due to atelectasis.

GROUP II

(Cases in which the Diagnosis of Hyaline Membrane was Considered but Excluded by the Help of X rays)

Case 12—Lower-segment cæsarean section at 37 weeks for maternal diabetes. Birth weight 8 lb. 2 oz Inspiratory recession was marked during the first 36 hours but spirometry showed improving minute volume and radiography at 30 minutes showed full expansion which was confirmed 21 hours later

In view of the well known tendency of hyaline membrane to develop after cæsarean section for maternal diabetes this information was valuable

Case 13—Breech delivery at 26 weeks. Birth weight 1 lb 11 oz. *At birth the baby was toneless and shocked* Respiration was augmented intermittently until the age of 11 hours. Condition remained satisfactory until 24 hours, when cyanosis developed Death took place suddenly at 32 hours. Radiography at 6 hours showed clear lung fields, and post mortem showed negligible pulmonary aeration and absence of bronchial tree markings At necropsy there was only slight aeration of the right middle lobe anteriorly and the anterior borders of both lower lobes. On section the lungs were found to be immature and many of the alveoli were lined by cuboidal epithelium. There was no hyaline membrane Death was due to atelectasis, which was evidently secondary but not associated with hyaline membrane.

Case 14—Abortion at 26 weeks Birth weight 1 lb 10 oz Respirations were very shallow and were augmented until at 8 hours the condition was greatly improved, and baby was transferred to an incubator

Radiography at 12 hours showed no evidence of pulmonary consolidation nor deflation Death occurred at 26 hours from intraventricular hæmorrhage The lungs showed only partial aeration (about 50%), and on microscopy atelectasis appeared almost complete except for groups of alveoli near the surface of the upper lobes. Many alveoli contained acidophil debris but without hyaline membrane

Case 15—Abortion at 27 weeks Baby cried at birth, but immediately became grey Aspirated, and respiration was augmented during first 3 hours because atelectasis was obvious Condition improved considerably, and radiography at 3 hours showed fairly good expansion and no evidence of collapse Transferred to incubator at 3 hours Died at 8 hours At necropsy the upper lobes were quite well aerated, but the lower lobes sank There was no hyaline membrane, and death was due to intraventricular hæmorrhage

Case 16—First of twins aborted at 27 weeks Birth weight 1 lb 11 oz Baby was pink at birth and cried well, and there was only slight recession.

Radiography at $4^1/_2$ hours showed good pulmonary expansion, and at 22 hours "excellent expansion" From 20 hours onwards there were increasingly frequent attacks of cyanosis, and the baby died at $38^1/_2$ hours At necropsy all the lobes floated, and on microscopy small areas of collapse were seen alternating with areas of over-distension. Hyaline membrane was absent, apart from an occasional minute fragment Death was due to intraventricular hæmorrhage

Case 17—Delivered at 32 weeks Birth weight 3 lb 12 oz Condition was good at birth, but there was subcostal inspiratory recession

Radiography on the first and second days of life showed full expansion Death took place at 46 hours Intraventricular hæmorrhage was found at necropsy, but lung expansion was very good, and there was no sign of hyaline membrane

Case 18—Second of twins. Forceps delivery at 34 weeks for maternal eclampsia at full dilatation Birth weight 3 lb 9 oz Consistently poor minute volume Respirations were augmented with some improvement

Radiography at 13 hours showed good aeration of both lungs, but death took place at 51 hours At necropsy a large tentorial tear was found. The lungs floated but were congested, and there were patchy alveolar hæmorrhages There was no hyaline membrane, but there was widespread patchy pneumonic consolidation.

Case 19—Delivered at 32 weeks Condition at birth was very good Birth weight 3 lb Spirometry at 15 minutes showed a minute volume of 333 ml with the baby quiet, and 827 ml with the baby crying At 1 hour the baby, during a burst of crying, achieved a minute volume of 1500 ml

Radiography at 1 hour 5 minutes and $4^1/_2$ hours showed good pulmonary aeration, although in the earlier stage there was some crowding of the markings at the base on both sides The signs did not resemble those we have come to associate with hyaline membrane The second radiograph showed improved expansion on the left but no change on the right The child survived

GROUP III

(Negative Radiological Signs with Hyaline Membrane found at Necropsy)

There have been no cases in this group to date

GROUP IV

(Radiological Changes Present but Infants Lived and Hyaline Membrane therefore Not Proven)

Case 20—Delivered at 32 weeks Birth weight 3 lb 8 oz Severe atelectasis, but minute volumes improved spontaneously during first two days Radiography at 2 hours showed coarse mottling, which had mostly cleared on radiography at 16 hours Radiography on the third day showed no mottling at all The baby recovered

Case 21—Rapid delivery at 28 weeks Birth weight 2 lb 15 oz Condition at birth good, but grunting and subcostal recession developed within 50 minutes.

Radiography at 1 hour showed incomplete expansion of right upper and middle lobes, with some fine mottling consistent with alveolar collapse Spirometry at 65 minutes showed a minute volume of 234 ml Respiration was augmented, and minute volume rose to over 600 ml. 50 minutes Further radiography at 7 hours showed expansion in the right upper and middle lobes. The since done well.

Case 22—Delivered at 33 weeks Birth weight Colour bad and atelectasis gross Respiration and minute volume slowly improved from 242 ml at 11 hours, with quiet respiration Child has although some degree of sternal recession persisted 48 hours

Radiography at $7^3/_4$ hours and $10^1/_2$ hours and outlining of the bronchial tree

Case 23—Delivered at 32 weeks after hæmorrhage Birth weight 3 lb 7 oz were grunting, and there was subcostal recession sisted for 2 days Minute volume of 507 ml. with the child quiet

Radiography at $1^1/_2$ hours (fig 9), 8 hours, and day, 4th day (fig 10), and 19th day (fig 11) mottling throughout at first which gave place to variety which in patches appeared somewhat confluent radiograph on the 19th day showed these changes disappeared The child has continued to do well.

GROUP V

(X-ray Changes Indicating Pulmonary Hyaline Membrane not Confirmed at N

Case 24—Delivered at 34 weeks Birth weight Initial condition good, but clinical signs of oped Minute volume 220 ml at 4 hours but 1100 ml after augmented respiration For the treatment was abandoned after two hours. attacks of cyanosis Death took place at 27 hours.

Radiographs taken at 4 hours, 8 hours, and death (fig 12), showed a very fine stippling and atelectasis These appearances became more each of the successive films At necropsy there intracranial hæmorrhage Pulmonary aeration appeared good Histology showed numerous the bronchioles, but there was no hyaline membrane. if the baby had lived longer, the recognised pattern of membrane might have developed Other illustrations case have been published (Donald and Lord 1953,

Case 25—Delivered at 26–28 weeks Birth weight Temperature on admission was 88°F, and there recession on inspiration Baby died suddenly, warning attacks of cyanosis, at 26 hours

Radiography at 7 hours showed very poor 20 hours some improvement, but there was

LEGENDS TO ILLUSTRATIONS ON

MR DONALD AND DR STEINER

Fig 1 (case 1)—Aged 3 hours. Fine mottling gesting alveolar collapse.

Fig 2 (case 1)—Aged 8 hours. Coarse mottling and lower lobe

Fig 3 (case 3)—Aged 6 hours. Coalescent shadows and bronchial tree.

Fig 4 (case 3)—Post mortem Almost complete deflation lining of bronchial tree.

Fig 5 (case 9)—Post mortem Total bilateral collapse and tree not outlined

Fig 6 (case 11)—Aged 8 hours. Fine mottling and partial left lung

Fig 7 (case 11)—Aged 36 hours. Mottling and progressive left lung

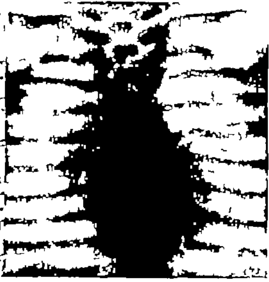
Fig 8 (case 11)—Aged 48 hours. Regression of signs of alveolar with some re-expansion of left lung

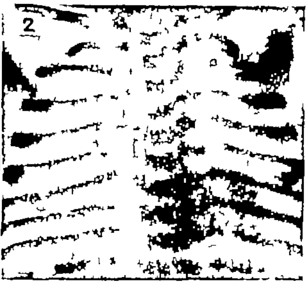
Fig 9 (case 23)—Aged $1^1/_2$ hours. Well-marked diffuse throughout lung fields

Fig 10 (case 23)—Aged 4 days. Mottling still present but patches rather confluent.

Fig 11 (case 23)—Aged 19 days. Clearance of radiological

Fig 12 (case 24)—Post mortem. Fine mottling collapse of left lower lobe.

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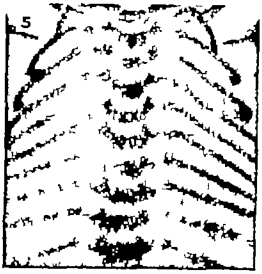
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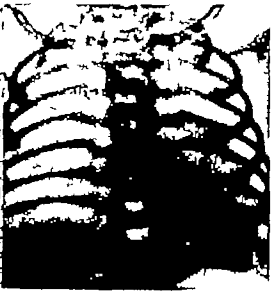

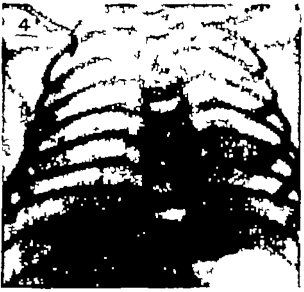
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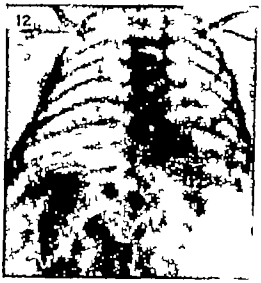
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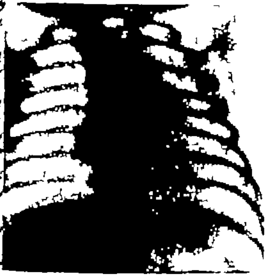

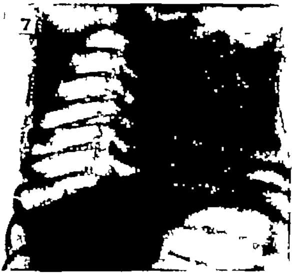
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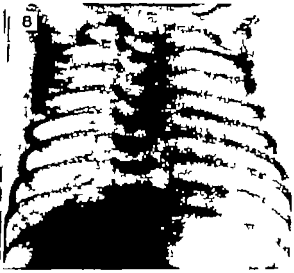
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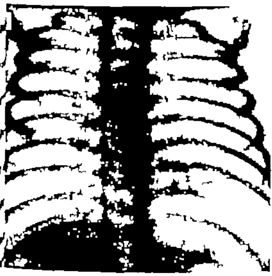

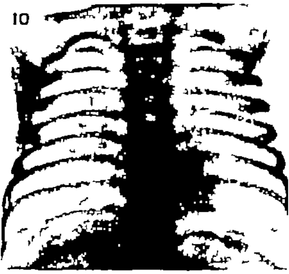
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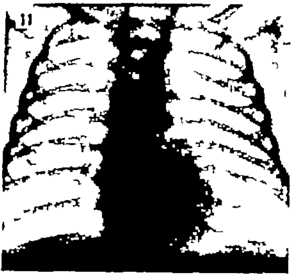
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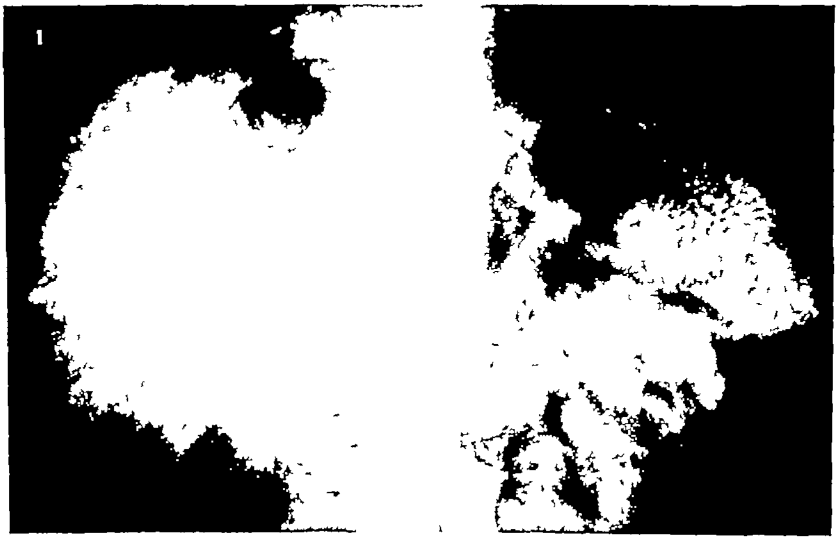
DRS BERENBAUM AND BIRCH THORIUM IN LIVER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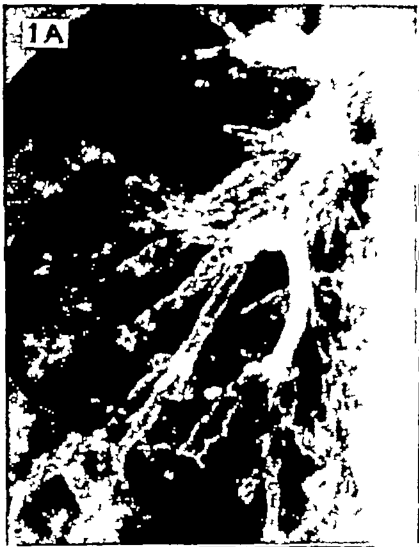
DRS SIMON AND GALBRAITH CHRONIC BRONCHITIS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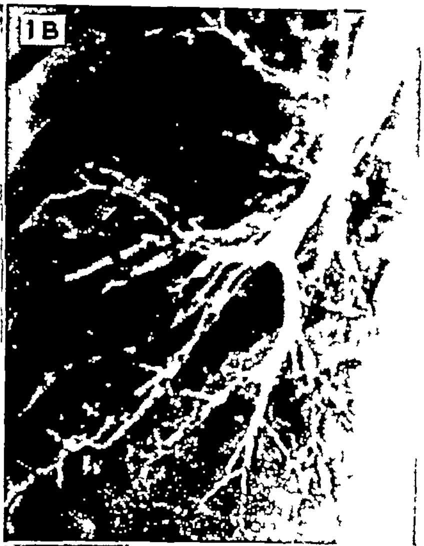
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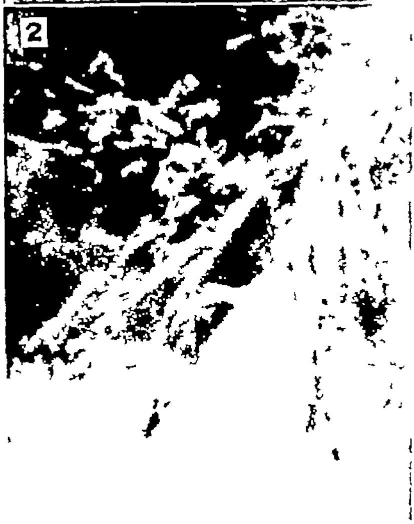
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DR RONALD
CAISSON DISEASE

2

tling throughout both lung fields and the bronchial tree not outlined as described in earlier cases. At necropsy nonary expansion was moderate and both lungs floated roscopy revealed no hyaline membrane Death was ibuted to pneumonic consolidation.

Vhen hyaline membrane is present collapse seems to gress from alveolar to lobar In hyaline membrane ase we have not so far seen this progression reversed reas in this instance pneumonia or primary atelectasis gressed from lobar to alveolar collapse and consolida The radiological sequence therefore appears to be ortant in the differentiation of the two conditions

ase 26.—Forceps delivery at 34 weeks for maternal mpsia at full dilatation First of twins Birth weight b 3 oz. Shocked at birth Respirations shallow with equent gasps Augmented respiration applied. Died at iours.

adiography immediately after death showed very poor ation on both sides No mottling was visible nor was the nchial tree outlined and we are inclined to regard this as ase of primary atelectasis. At necropsy all the lobes ted. Microscopy revealed overdistended alveolar ducts widespread areas of atelectasis but no hyaline mem ne Death was due to a large intraventricular hæmorrhage

ase 27.—Rapid delivery after antepartum hæmorrhage at weeks. Birth weight 2 lb 9 oz Recession developed and nosis deepened within an hour whereupon respiration was mented intermittently

adiography at 2 hours showed fairly good expansion of right lung but the left lower lobe was somewhat collapsed o mottling was visible throughout the lung fields. Although signs of recession had largely disappeared by $5^3/_4$ hours, ther radiography at this time showed the mottling to sist but the left lower lobe appeared better expanded diography at 20 hours and 48 hours showed further provement Nevertheless the child died at $4^1/_2$ days and necropsy the immediate cause of death was not determin o All lobes floated but there was some patchy emphysema hyaline membrane

this case either the radiographs gave a false positive ult or hyaline membrane was in fact present but olved before death

ase 28.—Delivered at 32 weeks Birth weight 2 lb 12 oz. mitted aged 1 hour Very little air entry could be detected, l recession was pronounced Radiographs taken at 9 hours hours and immediately after death showed good expansion the first film showed some very fine mottling At necropsy the lobes floated but the lower lobes were poorly aerated. rtial atelectasis was general but there was no hyaline mbrane Death was due to bilateral intraventricular morrhage

e radiological appearances in this case were not ll marked but might be classed as equivocal

Discussion

Different kinds of radiographic shadows are sometimes visible when hyaline membrane is present They represent a type of atelectasis associated therewith they are not specific of the lesion but tend to follow a definite sequence Three main types can be distinguished, all of which may be present at the same time or they may follow in quick succession in hours or days

At first fine miliary mottling more or less uniformly distributed throughout the lung fields is noticeable It appears within a few hours of birth and is probably due to diffuse alveolar collapse and alveolar consolidation. Caffey (1945) described a similar appearance and claimed that this was a physiological phenomenon in premature babies and represented small areas of atelectasis which called for no treatment and resolved within days or weeks He ascribed it to structural immaturity of the alveolar buds, citing Farber and Wilson (1933) We submit that these appearances are not physiological and we have traced their development in patients in whom hyaline membrane has been found at necropsy This mottling is not an attribute of prematurity per se, because clear lung fields are often demonstrable in unaffected premature infants. If the clinical course is progressive and down hill, this fine mottling becomes coarse and tends to coalesce Ultimately the shadows become confluent, until definite lobar or lobular consolidation and collapse are recognisable. If on the other hand, the condition improves, the initial mottling slowly resolves and ultimately the lung fields become clear In some instances all three shadows—miliary mottling coarse mottling and consolidation and collapse—are present in the same lung

Donald and Lord (1953) illustrated radiological changes of the above description without specifying at the time the radiological sequence of events and the diagnostic significance of these findings Meschan et al (1953) have described a further case and recommend an extended study

Once the coarse mottling has developed and areas of consolidation and collapse have appeared, the bronchial tree can at times be clearly seen outlined into its minor divisions particularly in the mid and lower zones This outlining of the bronchial tree is not found in primary atelectasis, when the lungs are totally opaque and only the trachea may be visible

The sequence of miliary mottling coarse mottling and lobar consolidation and collapse seems to be found only when hyaline membrane is present The reverse sequence of pulmonary collapse and subsequent resolution we have seen in pulmonary infection and in some cases of primary atelectasis

Summary

The assistance which radiology has to offer in the assessment of atelectasis of the newborn and the diagnosis of hyaline membrane during life is discussed.

Twenty-eight cases are described, from a study of which it appears that not only may diagnosis be clarified but also three distinct radiological patterns are discernible according to the stage of development of hyaline membrane.

The necropsy studies were made mainly by Dr A E. Claireaux, and we are indebted to him for his expert help Our thanks are due to Prof A Moncrieff for his continuing support and to members of the radiographic staff who have cooperated at all hours of the night This research is being assisted by a Leverhulme scholarship awarded to one of us (I. D) by the Royal College of Obstetricians and Gynæcologists

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LEGENDS TO ILLUSTRATIONS ON PLATE

DRS BERENBAUM AND BIRCH

1—Reticular distribution of radio-opaque substance in liver and plеen.

DRS SIMON AND GALBRAITH

1A (man aged 43)—Bronchogram of right lung during full nspiration

1B (same patient)—Full expiration showing change in calibre

2 (woman aged 50)—Bronchogram of right lung: arrow points o narrow area with dilatation beyond.

3 (man aged 50)—Bronchogram of left lung showing diverticulosis f left main and upper-lobe bronchi.

4 (man aged 49)—Bronchogram of right lung: arrow points to erry-like opacity ("peripheral pooling")

DR RONALD

1—Right humerus showing extensive necrosis with irregular bone regeneration cyst formation, and calcification.

2—Left tibia showing the formation of an "encapsulated infarct by the marginal calcification.

RADIOLOGY OF CHRONIC BRONCHITIS

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With illustrations on plate

As part of a clinical investigation of a large series of patients with chronic bronchitis (Oswald et al 1953), standard postero anterior chest radiographs of each patient were taken in suspended full inspiration The films of 857 of these patients have been studied with a view to determining whether there are any characteristic radiological features of chronic bronchitis, and whether there is any correlation between the clinical severity of the bronchitis and the presence or absence of any of the radiological signs commonly regarded as indicating emphysema

Bronchograms done in a representative group of 90 patients have also been studied

Review of Standard Chest Radiographs

Each radiograph was assessed by a radiologist (G S) who knew that the patients were suffering from chronic bronchitis, and (when he asked) was informed of their age and blood-pressure readings At the time of the assessment, he had no other clinical information

APPEARANCES SUGGESTING EMPHYSEMA

The criteria used for making a radiological diagnosis of emphysema were

(1) *A low flat diaphragm* —Owing to the film shortage at the time of these observations, only a single radiograph was taken in each case , hence the range of diaphragmatic movement could not be assessed

(2) *A narrow vertical heart with a prominence of the left border* just below the aortic knuckle, suggesting enlargement of the main pulmonary artery

(3) *An abnormal vascular pattern*—i e , clear prominent vessels in the region of the hila, which narrowed considerably after the early branchings in the lung fields These vessels were not only unduly narrow but appeared, as they proceeded distally, to be reduced in number compared with those seen in radiographs of normal persons, and they tended therefore to be abnormally widely spaced

(4) *Bullous changes* —A bulla was held to be present when a localised translucent area 1–10 cm in diameter, with a white hair line margin, was seen , and a bullous area was presumed when a poorly demarcated hypertranslucent area was seen without vascular shadows, or with a few apparently greatly narrowed vascular shadows within it

A radiological diagnosis of emphysema was made when all four signs were present, and occasionally when only the last three, including definite bullæ, were seen These criteria were satisfied in 128 (15%) of the whole series

Excessive visibility of large pulmonary vessels in the middle of the lung fields was not regarded as a sign of emphysema , nor was hypertranslucency of the whole or a part of the lung fields regarded as reliable evidence in the absence of the other criteria mentioned above The shape of the thoracic cage and calcification of the costal cartilages were ignored as factors in the diagnosis , in fact excessive calcification of the costal cartilages was noted with no greater frequency in those patients considered to have radiological emphysema than in the rest of the series

The patients who were thought not to have undoubted radiological evidence of emphysema could be subdivided into those with only some of the radiological featu emphysema and those with none (table I)

As part of the clinical investigation, these pa had been classified into six grades according to exercise tolerance , those in grade 0 had no dy grades 1, 2, and 3 had increasingly severe exert dyspnœa , patients in grade 4 were incapacitated dyspnœa on the slightest exertion , and those in gr were dyspnœic at rest The radiological appearance compared with the exertional capacities of the pa in table II, which shows a direct correlation between degree of dyspnœa and the frequency of the radiol demonstration of appearances suggesting emphy The presence of only some of the radiological suggestive of emphysema does not seem to have any relation to the exercise tolerance, which confirms belief of Knott and Christie (1951) that most of radiological signs said commonly to be associated emphysema “ if taken alone, are of doubtful diag significance ”

In some patients dyspnœa may have been due mo bronchospasm than to emphysema, and this may ac for the comparative infrequency with which a radiol diagnosis of emphysema was made in the incapac patients Another probable explanation is the con tive manner in which the radiological appearances assessed, the criteria described above being st adhered to It is also possible that small emphysem spaces, which often involve only primary or seco lobules (Reid 1953), may be invisible on a radiogr even if collectively they occupy a considerable

TABLE I—INCIDENCE OF RADIOLOGICAL FEATURES SUG EMPHYSEMA IN 857 PATIENTS WITH CHRONIC BR

—	No of pa
Undoubted radiological evidence of emphysema	128 (1
Some radiological features only insufficient to justify a diagnosis of emphysema	320 (3
No radiological features of emphysema	409 (4

OTHER RADIOLOGICAL ABNORMALITIES

Table III shows that in this group of patients chronic bronchitis radiological changes other than suggestive of emphysema were rare

The term “ inactive pulmonary tuberculosis ” w to signify small circumscribed dense or calcified confined to a small part of the lung, usually in the zones

The commonest pleural abnormality was “ thicken often with an overlying rib resection denoting empyema The high incidence of pleural abnorm may be related to the large number of chronic bronch whose symptoms date from an acute pulmonary infe and to the frequency with which pneumonia compli chronic bronchitis In 7 of the 11 patients with segme or patchy consolidation there was no obvious cons tional upset and the radiological opacities disapp within a few weeks , these patients (0 9% of the series) presumably had localised aspiration pneu of the type described by Scadding (1951)

The radiographs of the two patients with sponta pneumothorax, which had caused no symptoms in e case, showed generalised emphysema

NORMAL RADIOGRAPHS

Of the whole group of 857 radiographs 354 (4 were considered to show no abnormality in the fields

Bronchographic Appearances

Bronchograms were done in 90 patients who form representative group of chronic bronchitics. Fewe

LE II—COMPARISON OF RADIOLOGICAL APPEARANCES WITH EVERITY OF DYSPNŒA IN 857 PATIENTS WITH CHRONIC RONCHITIS

idence of radiological appearances in each clinical grade is expressed as percentage)

—	104 patients with no dyspnœa (grade 0)	304 patients with dyspnœa on heavy work (grade 1)	248 patients with dyspnœa on hurrying (grade 2)	154 patients with dyspnœa on walking (grade 3)	47 patients incapacitated by dyspnœa (grades 4 and 5)
iological em ysema	5	7	20	25	26
o radiological atures of em ysema	37	38	34	44	32
radiological atures of em hysema	58	55	46	31	42

ients were examined by bronchography than by ndard chest radiography but the distribution of ical severity and the sex incidence were comparable he two groups

VARIATION OF BRONCHIAL CALIBRE

Normally on respiration the bronchi vary in calibre oming wider on inspiration and narrower on expira- In 77 of the bronchograms films were taken in pended full inspiration and expiration to demonstrate range of variation In 2 bronchograms both of men h incapacitating chronic bronchitis generalised exces inspiratory dilatation was seen, the expiratory nchial calibre being normal. In bronchograms of 21 er patients similar excessive variation in calibre was n involving only a part—usually one or more mental branches—of the bronchial tree (figs 1A B)

Our experience of the bronchographic appearances on piration and expiration in normal people is inadequate, are the published references to this subject but ually even with the maximal respiratory movements variation is slight and the inspiratory calibre of medium-sized bronchus does not exceed one and a f times the calibre on expiration In these chronic nchitics considered to show excessive variation the piratory calibre was usually at least twice the expira y calibre, but admittedly accurate measurements are possible Chronic bronchitics especially those with ch dyspnœa, are not good subjects for bronchography l under these conditions it was often difficult to obtain isfactory respiratory excursions had this not been a higher incidence of excessive variation in bronchial ibre might have been observed and also a more wide- ead distribution of such changes throughout the nchial tree

BLE III—INCIDENCE OF RADIOLOGICAL ABNORMALITIES OF UNG FIELDS EXCEPT THOSE SUGGESTING EMPHYSEMA IN 857 CHRONIC BRONCHITICS

Radiological abnormality	No of patients showing abnormality
ctive pulmonary tuberculosis	61 (7%)
normal pleural shadows	50 (6%)
neycomb or "tubular" shadowing	12 (1 4%)
ar shadows (localised fibrosis)	12 (1 4%)
mental or patchy consolidation	11 (1 3%)
neralised reticulation	4 (0 5%)
ntaneous pneumothorax	2 (0 %)

BRONCHIAL DILATATION

In the bronchograms referred to in the last paragraphs the bronchial calibre on expiration was normal in 19 bronchograms however, there was local bronchial dilatation which persisted throughout both phases of respiration In 14 of these patients the appearance of the dilated bronchi was unusual, an irregular beaded appearance being produced by short and usually unequal segments of alternate dilatation and narrowing (fig 2) This beading was most frequently seen in one or more of the medium sized bronchi of the lower lobes, and was usually associated with absence of filling of the minor branches of the affected bronchus The incidence of these lesions bore a closer relation to the duration of the bronchitis than to its severity from this and from their localisation it seems possible that they result from past minor aspiration pneumonias being similar to some of the persistent bronchial changes which Morle and Robertson (1953) described as a sequel to such episodes In 4 patients a local cystic dilatation of one branch of an upper lobe bronchus was seen probably representing past tuberculosis A local dilatation of the left upper lobe and lingular bronchi which was seen in the films of 2 patients was unusual in that transverse striations were present, due to ridges in the bronchial lining

BRONCHIAL DIVERTICULOSIS

The commonest abnormality was diverticulosis of the main or of the lobar bronchi which was present in 45 (50%) of the bronchograms (fig 3) These outpouchings of the bronchial lumen were multiple and were usually seen on the inferior surface of the bronchi especially those of the upper lobes and lingula They are due to dilatations of the ducts of mucous glands (Reid 1953 Duprez and Mampuys 1953) One of the first accounts of bronchial diverticulosis by Morlock and Pinchin (1933) described in the same chronic bronchitic "dilatation of the trachea and the whole bronchial tree" with "irregularity of the smaller bronchi shown by beading" Bronchial diverticulosis occurs rarely if at all in bronchograms of normal people, and if seen diffusely in bronchiectatic patients it probably signifies a coincident generalised bronchitis

BRONCHOGRAPHIC EVIDENCE OF EMPHYSEMA

In only 1 patient had the iodised oil entered an emphysematous bulla but in 11 patients the bronchial pattern was distorted by bullæ. A common appearance which seems to bear a direct relation to other radiological evidence of emphysema was the termination of the iodised-oil pattern peripherally in small berry like opacities about 1–3 mm in diameter for which the name "peripheral pooling" is suggested (fig 4) Peripheral pooling was seen in 14 (67%) of the 21 bronchograms of patients whose standard radiographs suggested emphysema, and in only 12 (17%) of the 69 other bronchograms Absence of filling of the small peripheral bronchi was noted in many of the bronchograms, often distal to bronchi showing beading or distal to otherwise normal bronchi at the bases, which are the parts of the lungs where filling with iodised oil is usually most adequate In most cases this appearance was probably due to disease in the bronchioles but as such absence of filling may be due to technical failure, no accurate estimate of its incidence is possible

SPIDER BRONCHI

Generalised narrowing usually only apparent [illegible] to the third or fourth generation of bronchi was [illegible] in 4 bronchograms in none of these patients [illegible] bronchospasm severe A similar appearance [illegible] occasionally in normal people and its [illegible] is uncertain

TABLE IV—INCIDENCE OF PRINCIPAL BRONCHOGRAPHIC ABNORMALITIES IN 90 CHRONIC BRONCHITICS COMPARED WITH SEVERITY OF DYSPNŒA

(Expressed as percentages of patients in each clinical grade showing abnormality)

Clinical grade	Excessive variation of calibre	Diverticulosis	Localised bronchial dilatation	Peripheral pooling
15 patients with no dyspnœa (grade 0)	23	33	13	20
63 patients with dyspnœa on exertion (grades 1, 2, and 3)	31	52	19	29
12 patients incapacitated by dyspnœa (grades 4 and 5)	33	58	42	42

INCIDENCE OF BRONCHOGRAPHIC ABNORMALITIES

Table IV compares the incidence of the principal bronchographic abnormalities in the three clinical grades of dyspnœa In each case the incidence rises as the degree of dyspnœa increases 71 patients (79%) had some bronchographic abnormality, and in many, especially those more severely affected, more than one abnormality was present

Discussion

Chest radiographs are essential in the diagnosis of chronic bronchitis, because patients with other serious chest diseases often present with symptoms of this condition Once the clinical diagnosis of chronic bronchitis has been established, the value of chest radiography is less certain This study of single standard chest radiographs shows that, except for occasional minor changes, the only abnormalities are those which are commonly regarded as indicating emphysema The difficulties of the radiological diagnosis of this condition have been discussed by Knott and Christie (1951) In this survey we have insisted on three particular radiological signs—a fourth being often present in addition—before a radiological diagnosis of emphysema was made According to these criteria a direct correlation between the degree of dyspnœa and the frequency of the radiological diagnosis of emphysema has been found This suggests that the strict application of these criteria may be of value in the diagnosis of emphysema

Although in chronic bronchitis abnormalities are seen more frequently on bronchograms than on standard chest radiographs, bronchography is of less clinical value Lesions such as gross bronchiectasis and, more rarely, bronchial carcinoma can be excluded, and some estimate can be made of the degree of permanent damage present, this may be of importance if the surgical treatment of emphysema is further explored The bronchographic findings do not provide much help towards the understanding of the increased sensitivity of the bronchial tree in chronic bronchitis or of the causes of the disabling dyspnœa Reid has emphasised that the irreversible pathological changes which take place in advanced stages of chronic bronchitis affect chiefly the peripheral parts of the bronchial tree Her work confirms the important pathological significance of our bronchographic findings, the most remarkable of which are the "peripheral pooling" and the distortion and poor filling of the small peripheral bronchi and bronchioles

Summary

Standard chest radiographs of 857 patients with chronic bronchitis were examined

128 patients (15%) had radiographic changes suggestive of emphysema, the occurrence of such changes being directly related to the degree of dyspnœa Radiological evidence of emphysema was seen in only 26% of the patients who were incapacitated by dyspnœa The [illegible] used to make a diagnosis of emphysema were a low flat diaphragm, a narrow vertical heart with nence of the pulmonary artery, an abnormal pe vascular pattern, and evidence of bullæ

In 320 patients (37%) some of the radiological malities associated with emphysema were noted, appearances were not thought to be sufficient to a radiological diagnosis of emphysema

No other appearances which might be characteris chronic bronchitis were found, and in 354 (41%) of films there were no abnormalities in the lung fields

Bronchograms of 90 patients with chronic were examined, of which 79% showed some abnor The principal abnormalities were excessive varia the bronchial calibre on respiration, localised bronchial dilatation, bronchial diverticulosis, "peri pooling," and poor filling of the smaller bronch bronchioles

The value of standard chest radiographs and br grams in the diagnosis and assessment of p chronic bronchitis is discussed

We wish to thank Dr Neville Oswald for the of studying the radiographs of patients with chronic br seen in his clinics at Brompton and St Bartholo Hospitals

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THORIUM DEPOSITS IN THE LIVE

DEMONSTRATED DURING LIFE

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L R C P E, D C P
REGISTRAR IN PATHOLOGY

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With illustration on plate

THE fact that a thorium sol injected into an made the liver and spleen opaque to X rays was discovered by chance in 1929 by a Japanese w Oka (1930) Radt (1930) prepared a thorium dio which became available for clinical use under the 'Thorotrast' It is a suspension of thorium d (about 200 mg per ml) with an average partic of 3–10 mμ Reports were published on its us hepatolienography, retrograde pyelography, and graphy

Thorium in the Body

Intravenously injected thorium dioxide is taken up the reticulo endothelial system and slowly excreted the kidneys Thorium salts may also be excreted the bile (Salerno and Mattis 1951)

Thorium and its decay products are radioactive emit alpha and beta particles and gamma rays. emissions damage living tissues by producing in their path (Zirkle 1936, Lea 1947) From the follo table (adapted from Zirkle 1933) it is seen that practical purposes, and so far as internally depo radioactive substances are concerned, only alpha p need be considered

	Range in tissues	*Track* (ion pairs
Alpha particles	30–50 μ	40
Beta particles	0 5–5 0 mm	150
Gamma rays	Comparable to X rays	

The metabolism of injected thorium is complicat the fact that its decay products differ from it chem othorium 1 and thorium X are isotopic with radium like it, are deposited mainly in the inorganic roxyapatite lattice of bone, or tend to migrate there ormed elsewhere Thoron is a gas and enters the od About 0 1% is excreted by the lungs, the rest ntegrating rapidly to thorium A before this can open (Aub et al 1952) However most of the alpha ticles are released and most of the damage is done, he liver spleen, and bone marrow

he biological effects of radiation include severe or ial biochemical disorder inheritable change and plasia (Duggar 1936 Lea 1047 Bloom 1048 Tansley al. 1948, Dale 1951) Nevertheless thorium compounds pite warnings about their radioactivity (*Journal of American Medical Association* 1937 Taft 1937a) e been used diagnostically for many years Whitaker al (1033) limited its use to moribund patients and to se where the risks were overshadowed by its value in gnosis They demonstrated thorotrast granules in Kupffer cells and in scattered granules between the enchymal cells the long term effects were not died Willis (1048) said :

> While no tumours following the use of thorotrast in man e yet been reported, the risk that such may appear during next decade or so when due time has elapsed following use of this relatively recent method of diagnosis must be gnised "

elbie (1938) found that 40% of rats injected with rotrast developed sarcomata Thomas et al (1951) iewing the literature and addressing a questionary 167 radiologists were able to describe only 5 instances malignant growths following the injection of thoro at they concluded that this did not indicate a cinogenetic effect in man, but they thought that osis in the liver and spleen and at the site of an ravascular injection was a risk which made the use thorotrast unjustifiable They do not give details of ases (2 of liver tumour and 1 of leukæmia) but the er 2 can be summarised as follows

woman, aged 40 was given intravenous thorotrast 75 ml investigation of a lump in the liver diagnosed later as a oma (MacMahon et al 1047) For twelve years she ained normal. When she died at the age of 70 she was nd to have a hæmorrhagic primary endothelial-celled oma of the liver This arose in relation to the largest ount of thorotrast in the body Many of the tumour cells tained thorotrast.

similar appearance was noted by Rigler et al (1935) person with a primary liver tumour who was given an ection of thorotrast)

man, aged 48 had retrograde pyelography done with rotrast 30 ml Sixteen years later a spindle-celled sarcoma he kidney was found at operation. There was a massive ount of thorotrast next to the tumour

is is a rare renal tumour but the usual one found in mals after the injection of thorotrast It was therefore that thorotrast had caused the growth in this case llinger 1949)

Abrahamson et al (1050) reported the case of a patient o died with bilateral alveolar-celled carcinoma of the gs sixteen years after an injection of thorotrast 75 ml e liver and spleen contained thorotrast but thorotrast s not demonstrated in the lungs which were not lioactive and we do not think a causal relation p has been shown between the thorotrast and the cinoma.

pler et al (1017) reported a case of aplastic anæmia lowing intravenous administration of an unknown e of thorotrast nine years previously At necropsy marrow showed aplasia and deposits of thorotrast. orium dioxide constituted 5% by weight of the rrow Since the active marrow of an adult weighs out 700 g (Wintrobe 1051) this implies the presence the marrow of 35 g of thorium dioxide and an initial ection of at least 175 ml of thorotrast However irregularity of deposition may explain the high concentration of thorium in the sample of marrow examined Sections of the liver from this case were examined by Yagoda (1040) by autoradiography Calculations based on these studies showed focal concentrations of 3% of thorium dioxide

Schmidt et al (1050) mention a patient who had an unstated amount of thorotrast injected for cerebral arteriography and ten years later developed aplastic anæmia Deposits were shown radiographically in the marrow spleen and lymph nodes, but their radioactivity was not demonstrated.

The presence of radioactive substances in a living person may be shown by detecting radioactive gases (radon or thoron) in the breath (Martland et al 1025) thorium X in the fæces, or gamma rays emitted from the body (Taft 1037b) A full account of the elaborate methods used is given by Aub et al (1952) Autoradiography however is a method practicable in any pathology laboratory by means of which radioactive deposits may be demonstrated in tissues obtained by biopsy or necropsy

In the following case the diagnosis was confirmed during life

Case-history

A bachelor aged 52 was first seen in November 1952 Twenty three years previously thorotrast (probably 10 ml) had been injected into the arteries of the right leg in the investigation of some arterial disease for which the leg was later amputated. He remained well and active after this apart from bouts of "indigestion"—i.e attacks of upper abdominal pain which, he thought followed emotional upsets

On examination the liver edge was just palpable but the spleen could not be felt All the investigations made were negative except that films taken during cholecystography (which was normal) showed the liver and spleen to be full of a fine dense radio opaque substance giving a fine reticular appearance (fig 1) Radiography of the skeleton showed no abnormalities.

HISTOLOGICAL FINDINGS

Needle biopsy of the liver was performed the aspirated tissue being fixed in formalin and embedded in paraffin wax Sections showed liver of normal architecture but containing scattered deposits (about 20 in an area of 2 5 sq mm) Most of the deposits filled the cytoplasm of what appeared to be groups of 10–20 parenchymal cells but possibly these were clusters of swollen Kupffer cells (fig 2) Occasional deposits filled single parenchymal cells or Kupffer cells. Considerable amounts lay in the portal tract connective tissue which was fibrotic Small deposits lay freely between liver cells or in sinusoids, although this appearance may have been due to material shifted by the microtome knife The deposits were sharply outlined finely granular greyish, translucent and refractile. A few tiny granules were scattered throughout the tissues without forming discrete masses There was neither excessive cellular infiltration nor architectural disorganisation but all the nuclei of the parenchymal cells showed an

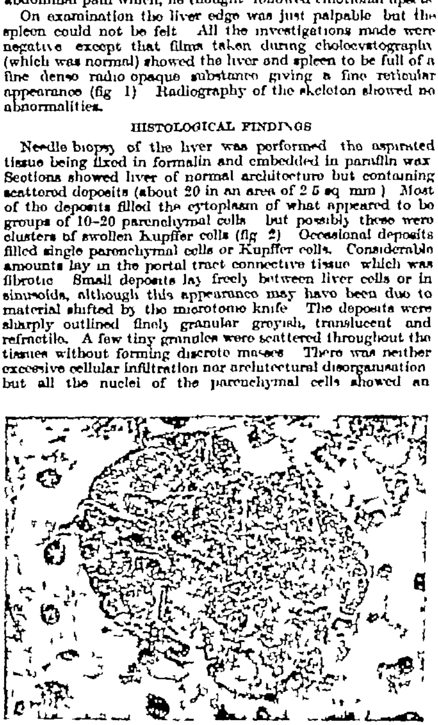
Fig 2—Deposit of thorium dioxide in liver cells. (Saffranine. × 1236.)

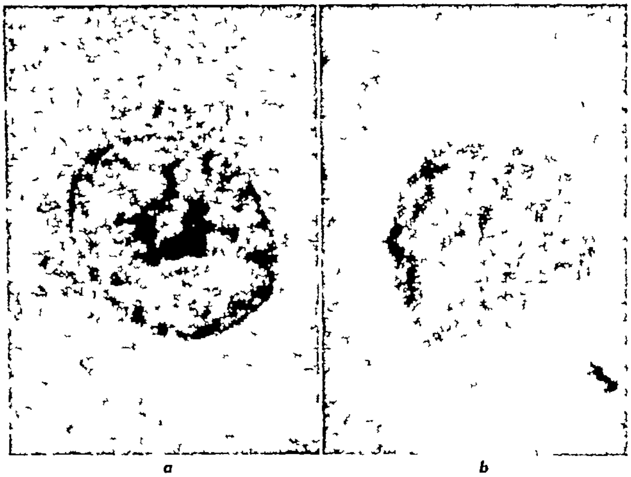

Fig 3—a, Normal liver-cell nucleus showing stringy chromatin in colourless nucleus sap and bounded by well-demarcated nuclear membrane b, abnormal liver-cell nucleus containing granular chromatin and bounded by abnormally thin nuclear membrane (Feulgen × 8000)

abnormality which may be significant The normal liver cell nucleus shows a sharply defined varicose chromatin network suspended in a colourless nuclear sap (fig 3a) The nucleolus is generally surrounded by a conspicuous condensation of chromatin, the "nucleolar associated chromatin," said to be concerned with the synthesis of protein (Thorell 1947, Caspersson 1947) In the present case the nuclei were uniformly filled with a fine peppery granular chromatin (fig 3b) The nucleolar associated chromatin was generally diminished in amount The nuclear membrane was abnormally thin

On the whole, the nuclei were slightly smaller than normal, particularly those of the cells containing deposits, but it is difficult to be certain of this in routinely processed material Though these changes could be appreciated with any nuclear stain, they were best shown by the Feulgen technique (fig 3) No mitotic figures or cytoplasmic abnormalities were seen

We have not seen such a strikingly uniform abnormality in any of the numerous other liver biopsy specimens which we have studied In particular the nuclei of pyknotic liver cells, which they most resemble, are much more uneven in distribution and show much more irregularity in staining and outline

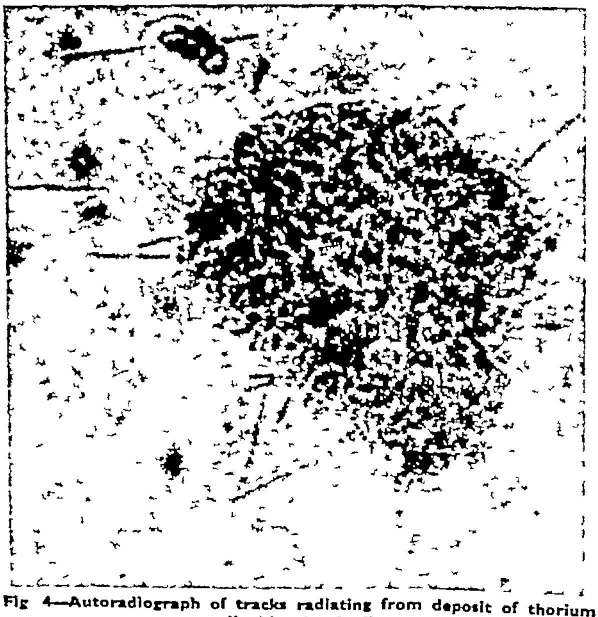

Fig 4—Autoradiograph of tracks radiating from deposit of thorium dioxide (× 1236)

Abundant glycogen was present, even in on those containing deposits, although it could demonstrated in these However, chemically glycogen may show a considerable decrease before apparent histologically (Morrione and Mamelok

RADIOACTIVITY

The radioactivity of these deposits was by using alpha-track plates, in which the produced by the passage of an alpha particle silver bromide, rendering the track visible after ment of the plate (For a full discussion see 1949, Doniach and Pelc 1950, Heller 1951) The of Endicott and Yagoda (1947) was followed.

Paraffin sections 3 μ thick were mounted on emulsion, and the plates were stored for twenty The wax was then removed, the plates were and the sections were stained with Meyer's and mounted in D P X mounting medium

A typical result is shown in fig 4, in which radiating from the deposit are seen in the About 100 tracks are seen per section This about half the alpha particles emitted, the other travelling away from the emulsion

The amount of thorium in the liver can be calculated, on the assumption that the deposits thorium in equilibrium with its decay products, and the biopsy is a fair sample of the liver, as follows

Volume of section	= 0 0075 c.mm.
Equivalent volume of unfixed liver	= 0-0125 c.mm. based on
Number of sections in a liver 1500 c cm in volume	= 1 20 × 10'
Number of alpha particles emitted in liver in 20 days	= 2 40 × 10''
Number of alpha particles emitted by thorium 1 g in 20 days	= 4 34 × 10''
Mass of thorium in liver	= 0 55 g

This is equivalent to thorium dioxide 0 63 g or thorotrast

If the original injection was 10 ml , this indicates 30 % of the total dose remains in the liver at Jacobson and Rosenbaum (1938), basing their lations on gamma-ray measurements, found that of injected thorotrast remained in the liver after years

In the present case, therefore, the liver has shown to contain radioactive deposits, and deposits may be presumed to be present in the (which was radio-opaque) and bone-marrow We say with certainty whether the nuclear changes represent radiation damage or not

Bloom (1948) irradiated numerous species of animals various external and internal sources He observed of chromatin and increased clarity of nuclear detail. ever, his experiments, like many others which have published, were short term and involved relatively radiation

Tripoli (1934) observed pyknosis of liver nuclei in but only when ten times the standard dose was photomicrograph of the liver in a case reported by and Chase (1936) shows increased nuclear basophilia, similar photograph in the case reported by Jacobson Rosenbaum (1938) shows vacuolated nuclei In neither does the author comment on these appearances

In general, the photomicrographs hitherto of thorotrast deposits in man do not show any of the nuclei

Discussion

The dangers of the presence within the body of amounts of radioactive matter have often been demonstrated (Martland 1926, 1929, 1931, et al 1925) In spite of this it is still the practice of radiologists to give as much as 75 ml of (Pirkey et al 1951, Loeb et al 1952) This equivalent to 1–3 μg of radium (*Journal of the Medical Association* 1937) As an illustration of this amount of radioactive substance may the cases of chronic radium and mesothorium reported by Aub et al. (1952) may be considered

In their series there were 13 patients with a body of radioactive material equivalent to 0 5–3 0 μg of these 2 were crippled by pathological fractures and 1 eloped a giant-cell tumour of the jaw 1 an osteogenic oma and 2 a carcinoma of the nasal sinuses. The carci mas did not appear until more than thirty years after the tial exposure

ince thorotrast has been in general use for little re than twenty years it is not surprising that few ths attributable to its radioactivity have so far been orted. If a person dies of a malignant tumour unless quate histological examination of post-mortem tissues made, it will not be realised that the growth may be to a single injection received twenty years previously l perhaps long forgotten

There is much to be said for limiting the use of thoro st to shed light on difficult diagnostic problems in erly patients, where its use may prevent or expedite najor operation Pirkey et al (1951) who adopted se indications used it only seven times in 100 000 uninations.

Summary

Reports of thorotrast deposits in man mention 7 deaths ributable to the radioactivity of thorium

The doses of thorotrast commonly used are carcinogenic

The demonstration of radioactivity in tissues does t require expensive materials, special preparation the tissue, or elaborate technique. It should be empted whenever routine histological examination eals deposits which are possibly thorotrast or other lioactive material

In this way the difficulty of assessing the true incidence thorotrast-induced tumours in man might be ninished.

Our thanks are due to Dr R H Herz, of Kodak Research boratory for the alpha track plates and to Mr H. Knight the photographs.

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ASEPTIC NECROSIS OF BONE IN CAISSON DISEASE

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With illustrations on plate

CAISSON disease decompression illness, or the bends' develops when a person who has been working in an atmosphere of compressed air undergoes decompression too rapidly Excess nitrogen (in the form of bubbles) is released within the body causing tissue damage Bert in 1880 suggested that this was the mechanism involved and the work of Boycott Damant and Haldane (1908) and Bornstein (1910 1914) has since confirmed the hypothesis The clinical features are those of injury usually transient, to different systems—cerebrospinal (varying from paræsthesiæ to unconsciousness) cardiovascular (embolic) pulmonary (dyspnœa), visceral and urogenital (nausea vomiting and pain), dermal (pruritus and lividity) and skeletal (Erdman 1913) Affection of the bones is commonly associated with pain, often so severe as to produce the characteristic distortion of posture from which the name the bends originates

That permanent changes take place in the bones was shown by Bornstein and Plate (1911) and by Bassoe (1911 1913) independently when they described the radiological appearances of mottled changes in density in the head of long bones, with flattening of the articular surface, narrowing of cartilage space and marginal lipping The changes have since been recognised as those of aseptic bone necrosis (Coley and Moore 1940) The condition is not common and a case is reported here

Case report

A man, aged 62, was admitted to hospital with pain in the chest after a fall; he had also had discomfort in the left wrist He had been employed in Great Britain as a diver for more than forty years and had worked almost every day up to six hours, wearing a diving suit into which air was pumped from compressors on the deck above He had worked at depths of 60–80 ft He estimated that on the average he had periods of two hours submerged with short intervals for rest between In diving he reached 80 ft in about ten seconds coming up he stopped at 40 ft for ten minutes, 30 ft for ten minutes and 10 ft for fifteen minutes to decompress before surfacing

History of Bends

He had had the bends more or less constantly and at least once a week had a severe attack, usually on a Monday The attacks were of two kinds— bad and mild The bad type came on if he had been working deeper than 60 ft When he came into the fresh air he would develop a sick feeling in the abdomen, his face became greyish yellow and he had vague general pains followed by sudden agonising pains in the joints—e g shoulder and knee These pains were severe for an hour or two and gradually passed off in five or six hours. When they were exceptionally severe a local anæsthetic injected into the skin over the joints gave some relief. After the pains had disappeared the limbs were relatively anæsthetic and for some hours there might be some incoördination of walking In the mild type of attack which he called skin or plum pudding bends his whole body became blue-white and intensely itchy This was rapidly relieved by a very hot bath He could feel air bubbles under his skin This lasted about twenty four hours and he could hardly bear to have his skin touched because it was tender as well as itchy His trunk was particularly affected.

During his work he was usually examined medically once a year and he had worked considerably later in life than the average diver who usually gives up this work about the age of 50

Investigations

He was a well built man showing no evidence of distress and general clinical examination revealed no abnormality in the vascular nervous or other systems.

A *blood count* showed red cells 5,220,000 per c mm , Hb 100%, white cells 7500 per c mm , polymorphs 57%, lymphocytes 31%, monocytes 7%, eosinophils 5%, erythrocyte sedimentation rate 8 mm in 1 hour (Westergren) , Wassermann reaction negative

The *urine* contained no abnormal constituents and no excess of calcium (Sulkowitch test)

An *electrocardiogram* was within normal limits

Radiography showed no abnormality of the heart or of the lungs, but it showed intramedullary calcification of the lower end of each femur, the upper end of each tibia, and the upper end of each humerus The calcification started from the region of the epiphyseal line, extending thence into the shaft of the bone The cortex was not involved, and the bone was not expanded (figs 1 and 2)

Biochemical findings—Serum calcium 10 mg , serum-phosphorus 4 5 mg , serum alkaline phosphatase 4 2 units, serum acid phosphatase 2 0 units, and blood cholesterol 118 mg per 100 ml , calcium balance normal

Discussion

Aseptic necrosis of bone does not necessarily give rise to symptoms unless it involves the articular surface of a joint Its primary cause is interruption of the blood-supply, with subsequent death of bone It can be produced experimentally by the injection of irritants (Bancroft 1922), by mechanical blockage of vessels e g , with charcoal solution (Kistler 1934), by periosteal stripping (Brunschwig 1930), and by air embolism (Colonna and Jones 1948) Its production in caisson disease is perhaps slightly more complex than at first appears

When the body is subjected to compressed air, the fats and lipoids absorb five times as much nitrogen as do the non-fatty tissues The main deposits of fat are in the abdomen, central nervous system, and long bones The bone marrow and spinal cord are, in relation to the nitrogen content, the tissues with poorest blood supply, and they are enclosed in bone, which prevents the diffusion of nitrogen into the adjacent tissues If decompression takes place too suddenly, nitrogen is released in excess of what can be excreted by the lungs Nitrogen stasis occurs, with the formation of bubbles in the blood and tissues, particularly where the saturation is high or the blood flow slow—the sites already mentioned The cortex of the bones is spared by virtue of its rich blood supply, and the lesions are usually confined to the diaphyses, but metaphyseal and articular lesions can occur The location and severity of symptoms depend on the site affected and the volume of gas released

The gas bubbles have a mechanical action in both intravascular and extravascular sites in blocking the blood-flow Furthermore, compression tends to increase the intravascular agglutination of erythrocytes (James 1945), and this agglutination is intensified as the carbon-dioxide tension increases (Swindle 1937) The obstruction of the blood-vessels is completed by their inability to expand against the rigid walls of the bony tube in which they are confined Consequently infarction of the bone occurs

The changes which ensue take a considerable time to develop but nevertheless may follow even one faulty decompression The pathology is that of bone necrosis and infarction Within the shafts of the bones necrotic areas are found surrounded by a fibrous wall Calcification and ossification take place, and the place of the dead bone is partly taken by new bone (Kahlstrom et al 1939, Walker 1940) Radiography reveals an irregular area of increased density usually surrounded by a thin band of calcification The medulla beyond appears normal The lesions are multiple and restricted to the long bones

In the differential diagnosis must be considered chronic sclerosing osteitis (rarely multiple, and usually showing cortical thinning and medullary narrowing), sclerosing osteogenic sarcoma (pain, ill defined border, and of calcified boundary), calcifying enchondroma (
symmetrical, and expansile), syphilitic osteitis (pa
and serologic reaction), and tuberculosis (
new bone)

Treatment is directed towards the preventi
deformity and its correction if necessary The
can be prevented by adequate decompression

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USE OF ETHYLENE DIAMINE TETR ACETIC ACID (VERSENE) FOR REMOV FISSION PRODUCTS FROM THE SKELETON*

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O B E , D M Oxfd, F R C P

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M A , D Phil

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The presence of minute traces of radium in the
has long been recognised as a serious toxic hazard
cause blood dyscrasias and bone tumours (Martland
1925, Aub et al 1952) Hamilton (1947) has p
that a large number of the radioactive product
uranium fission are also selectively retained in
skeleton, while the strontium isotopes are " par exce
producers of bone tumours " (Brues et al 1946,
1949) The deposition of these radioactive is
appears to follow one of two patterns The deposit
strontium follows the same route as that of cal
(Kidman, Rayner, Tutt, and Vaughan 1952, J
Rayner, Tutt, and Vaughan 1953) The depositi
yttrium and the rare earths differs from that of stro
in that immediately after injection it is found in c
areas of active growth only (Hamilton 1947, R
Tutt, and Vaughan 1953)

Attempts to increase the normal extremely slow
such isotopes from bone proved disappointing (Vau
Tutt, and Kidman 1952) until an increased ur
excretion of yttrium in rats was reported (Forema
Hamilton 1951, Cohn et al 1953) following the adr
tration of calcium and sodium salts of ethylene di
tetra acetic acid (versene or E D T A) Ethylene di
tetra acetic acid is a chelating agent which has m
ability to form soluble complexes with cations in sol
Chelation occurs most readily with certain metal
as copper and lead and the rare earths On theo
grounds it should form a chelate with yttrium, wh
trivalent (Cabell 1952) The alkaline earths, su

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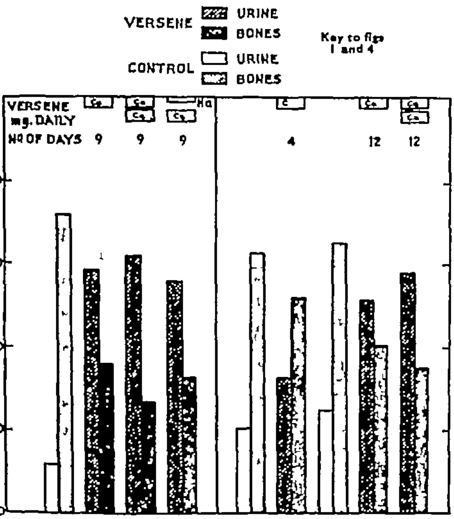
* This work was begun on behalf of the Protection
Committee of the Medical Research Council's Com
on Medical and Biological Application of Nuclear P



—Excretion and retention of ^{91}Y in rabbits (5–7 weeks old) following daily administration of versene.

um, are held less strongly No chelation occurs with h metals The sodium salt is known to be toxic to als (Bersworth Chemical Company 1952) though necessarily to man (Spencer et al 1952) since tion occurs with calcium following injection and calcæmia may result The calcium disodium salt he other hand, appears to be non toxic (Bersworth nical Company 1952, Spencer et al. 1952) and is lly excreted Preliminary observations suggest that salt is of value in treating lead poisoning both in lren and adults (Sidbury et al 1953)

e following report describes experiments on the tiveness of sodium and calcium ethylene diamine acetic acid in removing ^{90}Sr ^{90}Y and ^{91}Y from the ton of rabbits.

Experimental Procedure

abbits of the same stock as those used in previous riments (Kidman Tutt and Vaughan 1950) were in metabolism cages so that urine and fæces could be collected separately They were aged 5–7 weeks or over 12 months and were given a single intravenous injection of either ^{91}Y or ^{90}Sr–^{90}Y equilibrium mixture (25 μc per kg) This was followed by intraperitoneal injections of calcium disodium versenate or trisodium versenate at various intervals The dose given was an arbitrary one The young rabbits weighing 0·64 ± 0·02 kg were given 250 mg calcium disodium versenate or 120 mg trisodium versenate once or twice a day In one instance 30 mg of trisodium versenate was given an hour before the calcium salt The older rabbits weighing 2·45 ± 0·12 kg were given 500–750 mg calcium disodium versenate once or twice a day Only one control rabbit given no versenate was included in each group since the figures both for excretion and retention agreed well with those obtained in earlier experiments (Kidman et al. 1950 Rayner et al 1953 Jowsey et al 1953) In one experiment the control was given an intraperitoneal injection of physiological saline twice daily since no effect on excretion was noted this was not done in other controls

Estimations of excretion and retention of ^{91}Y and ^{90}Sr–^{90}Y were made as previously described (Kidman et al 1950 Tutt Kidman Rayner and Vaughan 1952) The amount of ^{91}Y excreted is throughout expressed as the total over the period of examination Excretion in the fæces was small and unaffected by treatment it was therefore ignored after the first few experiments. Retention in skin, flesh, and each organ was initially determined separately but again the amount was so small that it was subsequently also ignored

Autoradiographs were prepared by methods previously described (Kidman et al. 1952) except that all sections were ground to the same thickness (200 μ) after cutting on the milling machine and were exposed for the same length of time on standardised X-ray stripping film specially prepared by Kodak Ltd This standardisation of the technique allows of comparison of intensity of reaction between autoradiographs.

Results

EXCRETION AND RETENTION OF ^{90}Sr–^{90}Y

Sodium versenate given 1 hour after a single injection of ^{90}Sr–^{90}Y equilibrium mixture and then daily for a total of 9 days.—These rabbits (aged 5–7 weeks) showed no reaction suggestive of tetany but on some occasions following injection they appeared rather collapsed for a few minutes: weight gain was not impaired The excretion of ^{90}Sr in the urine of the control animal was 15·0% of the injected dose compared with 13·2% in the rabbits receiving the versenate Retention in the

EFFECT OF VERSENATES ON PERCENTAGE EXCRETION AND RETENTION OF ^{90}Sr AND ^{91}Y IN RABBITS

Method of Administration	Young (5–7 weeks)				Old (12 months and over)			
	Control		Versene		Control		Versene	
	Urine	Bone	Urine	Bone	Urine	Bone	Urine	Bone
versene 1 hour after ^{90}Sr and daily for 9 days	15·0	50·0	13 2	60 8				
versene 1 hour after ^{91}Y and daily for 9 days	1[illegible] 3 ± 0 7	72 9 ± 2 9	53 3 ± 1 2	36 0 ± 1 8				
versene 1 hour after ^{91}Y followed by CaNa$_2$ rsene daily for 9 days	1[illegible] 3 ± 0 7	72 9 ± [illegible] 9	56·2	3[illegible] 8				
versene 1 hour after ^{91}Y and twice daily for days	1 3 ± 0 7	72 0 ± 2 9	61 5 ± 2 7	20 0 ± 1 8	25 5	59 5	75 [illegible]	21 3
versene 2 weeks after ^{91}Y for 4 days	20 1	62 7	32 7	52 2			33 [illegible]	45 [illegible]
versene 2 weeks after ^{91}Y for 12 days once daily	[illegible]1 8	6[illegible] 4	51 7	40 3				
versene 2 weeks after ^{91}Y for 12 days twice daily	19 0	77 2	58·0	3[illegible] ± 1·6	37·07	59 3	51 11 ± 1 8	47·0 ± 3 [illegible]

bones of the latter was 60 8 %, while in the control it was 50 9 % ^{90}Y excretion was increased by administration of versenate as shown by examination of the restoration of the equilibrium concentration of ^{90}Y in the urine (Kidman et al 1950, 1951) No quantitative results were obtained, for the counter wore out before its efficiency relative to the isotopes concerned was determined

EXCRETION AND RETENTION OF ^{91}Y

Rabbits Aged 5–7 Weeks

(*a*) *Calcium disodium versenate given 1 hour after a single injection of ^{91}Y and daily for 9 days*—The animals excreted a total of 58 3 ± 1 2 % of the injected dose while the controls excreted 12 3 ± 0 7 % The bones of the control contained 72 9 ± 2 9 %, compared with 36 0 ± 1 8 % in the treated animals, retention in the carcase apart from the bones was 8 0 % in the control and 2 7 ± 0 2 % in treated animals (fig 1, table) Two animals received daily 30 mg of sodium versenate, followed an hour later by calcium versenate The total ^{91}Y excreted was not increased compared with animals receiving calcium versenate alone

(*b*) *Calcium disodium versenate given 1 hour after a single injection of ^{91}Y and twice daily for 9 days*—The rabbits showed no toxic reaction and gained weight The mean total urinary excretion ^{91}Y was 61 5 ± 2 7 % compared with 12 3 ± 0 7 % in the control The mean total retention in the skeleton was 26 6 ± 1 8 % compared with 72 9 ± 2 9 % in the control (table, fig 1)

Geographical autoradiographs prepared from longitudinal sections of the tibia fibula (fig 2) show a generalised reduced reaction throughout the whole bone in animals which had received versene compared with the control The most noticeable difference was in the region of the lower end of the metaphyseal trabeculæ No reaction was present in the autoradiographs prepared from bones of versene-treated animals, while a heavy reaction was present in the control

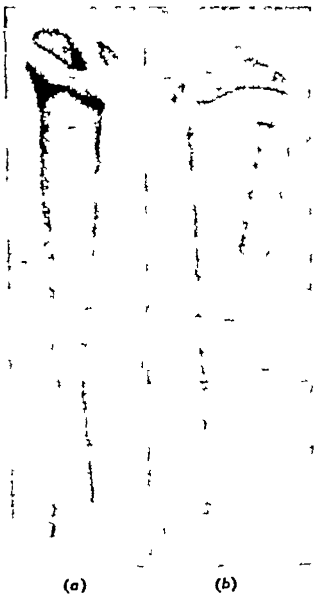


Fig 2—Geographical autoradiograph: longitudinal section of tibia of rabbit (5–7 weeks old) killed 9 days after a single injection of ^{91}Y (a) Control (b) Given an injection of versene one hour after ^{91}Y and twice daily for 9 days. Note (1) general reduction of reaction; (2) absence of reaction from metaphyseal trabeculæ.

(*c*) *Calcium disodium versenate given 14 days after a single injection of ^{91}Y each day for one period of 4 days Total period of collection 22 days*—There was a sharp increase in the daily ^{91}Y excretion in the urine after injection of versenate A total of 32 7 % of the injected dose was excreted by the treated rabbits, compared with 20 1 % by the control The skeletal retention was reduced from 62 7 % in the control to 52 2 % in treated rabbits (table, fig 1)

(*d*) *Calcium disodium versenate given 14 days after a single injection of ^{91}Y for a total of 12 days, divided into 4-day periods Total period of collection 38 days*—Each collection of urine after versenate injection showed an increased ^{91}Y content The total amount excreted was smaller in each successive The diminished response is only in part due decrease in ^{91}Y content of the bone (fig 5) total excreted was 51 7 % in the treated 24 8 % in the control, the total retained in the was 40 3 % in treated animals and 65 4 % in the (table, fig 1)

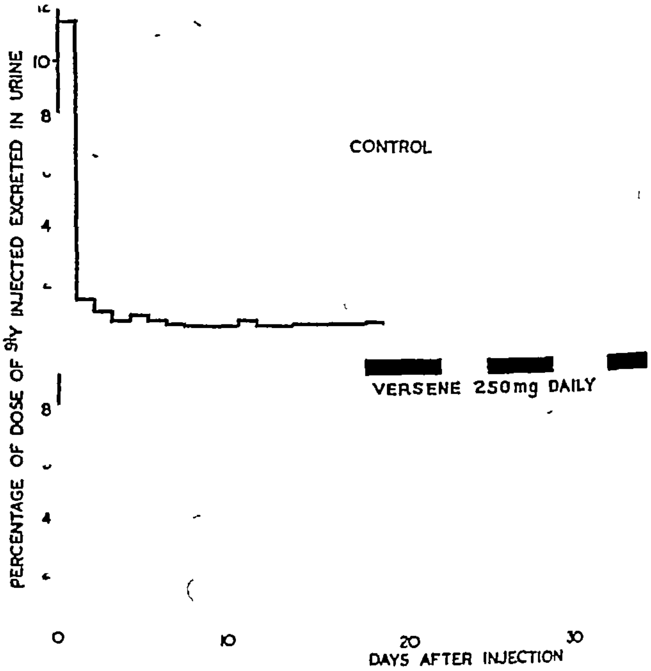


Fig 3—Average daily excretion of ^{91}Y in rabbits (5–7 weeks old) following inject

(*c*) *Calcium disodium versenate given 14 days single injection of ^{91}Y twice daily for a total of divided into 4-day periods Total period of 38 days*—The results were not greatly different those obtained in the series with single daily of versenate, although there was slightly more the urine The total urinary excretion was 5 the treated rabbits and 19 0 % in the control The skeletal retention was 35 2 ± 1 6 % in the treated and 77 2 % in the control (table)

Rabbits Aged 12 Months or Over

(*a*) *Calcium disodium versenate given 1 hour single injection of ^{91}Y twice daily for 9 days*—The total urinary excretion by the treated rabbi 75 2 % of the injected dose compared with 26 control, the skeletal ^{91}Y content was 24 3 % treated rabbits and 59 5 % in the control (table,

(*b*) *Calcium disodium versenate given 14 days single injection of ^{91}Y each day for 4 days Total of collection 38 days*—No rabbit was available to as a control in this experiment There was a increase in the urinary ^{91}Y output after inject versenate, but the increase was much less than case of the younger rabbits (fig 5)

(*c*) *Calcium disodium versenate given 14 days single injection of ^{91}Y for a total period of 12 day into 4-day periods Total period of collection 3*—The rabbits treated with versene excreted 51 1 ± 1 of the injected dose compared with an excret 37 1 % by the control, the skeletal content of 47 6 ± 3 4 % in the treated rabbits and 59 3 % control (table, fig 5)

In all animals injected with versene there adhesions and some inflammation of the abdominal In the animal receiving normal saline no such were seen.

Discussion

The experiments described suggest that disodium versenate is effective in increasing the

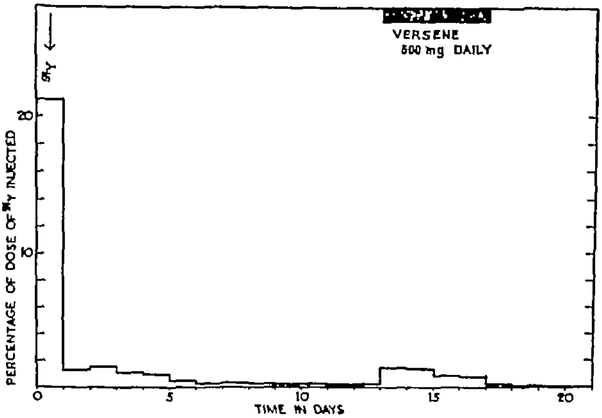
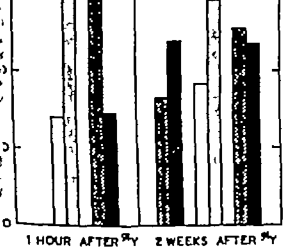


Fig 5—Average daily excretion of ^{91}Y in urine of rabbits (over 12 months old) following administration of versene.

and ^{91}Y, especially in young s but is without effect on the ion of ^{89}Sr This is not sing Calcium excretion is sed by the administration of n versenate (Spencer et al. but the stability constants of rontium and calcium complexes ersene are not sufficiently nt to allow preferential com g of minute traces of stron n the presence of considerable ties of calcium (Cabell 1952) effect on yttrium excretion eater in young than in old ls. The skeletal burden is ciably reduced in both age s if the versene is given imme y after injection of yttrium f it is given two weeks later ffect in the older animals is These differences may be ined by assuming that chela ccurs with the yttrium present e blood-stream immediately injection or released to the -stream by the normal process orption The great reduction d in the lower end of the metaphyseal trabeculæ of g rabbits treated with versene for 9 days compared the control suggests that the isotope is removed areas of high metabolic activity associated with d blood-supply In old animals metabolic activity e bone is slight and little yttrium is released to the -stream. The skeletal burden is therefore not ciably reduced

is difficult to understand why the administration o doses instead of one in each 24 hours has little upon the total amount of yttrium excreted.

atever the mechanism of the increased excretion, suggested that the administration of calcium nate to young people who may inadvertently ingest active yttrium and possibly the rare earths, offers some hope of reducing the skeletal burden particularly if given within 24 hours In man it should probably be given by slow intravenous transfusion (Spencer et al 1952 Sidbury et al 1953) The correct dose is still a matter for investigation †



—Excretion and retention of ^{91}Y in rabbits (over months old) following daily administration of sene.

Summary

Experiments are described on the effect of injections of calcium disodium and trisodium ethylene diamine tetra acetic acid on the excretion of certain bone seeking radioactive isotopes in rabbits

The calcium disodium salt appears non toxic and has a considerable effect on the excretion of radioactive yttrium in both young and old animals if given shortly after injection of the isotope. If given 2 weeks after injection it reduces the skeletal burden in young rabbits but not appreciably in older animals It is without effect on the excretion of radioactive strontium

This chelating agent may well be of therapeutic value in people who ingest certain bone-seeking isotopes.

We should like to express our thanks to Prof J H. Burn, F.R.S., whose constant help and encouragement has made this work possible. We are grateful to the Bersworth Chemical Company for a generous gift of calcium versenate. One of us (J M. V) has an expenses grant from the Medical Research Council We are also indebted to the Hæmatological Research Fund endowed by the Nuffield Foundation.

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tent experiments have shown that reducing the amount of ver e to 120 mg daily does not reduce excretion; reduction to mg daily reduces it to a moderate extent.

MALNUTRITION IN THE ELDERLY

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MUCH has been written about the effects of widespread starvation associated with political strife, war, and the great famines due to failures of crops such as are still seen in China and India today This paper deals with less dramatic circumstances of malnutrition which are not uncommon in general and hospital practice even in these islands, and which mainly affect the elderly

In the first half of this century nutritional research concerned itself so successfully with infants and children that rickets and infantile scurvy have become almost historic diseases We intend in this paper to show that there are opportunities for investigation of malnutrition in the aged, and that there may be need for fresh means of solving social and medical problems which are likely to grow in proportion to the ever increasing span of life

Diagnostic Criteria

Most of our statements are based on case-histories of patients in a general hospital which admits, mainly, but not exclusively, the aged ill Only patients who were under the personal supervision of both or either of us have been considered in this review, which comprises 39 patients of both sexes Only those in whom malnutrition was the primary and main disability were included In a number of patients we believed that reactivation of fibrotic phthisis, development of non-specific respiratory infections, or urinary sepsis, were in fact secondary to malnutrition Such cases were, however, not included, neither, of course, were such conditions as pernicious anæmia or malignant disease associated with malnutrition

In the course of 17 months, from May, 1951, until September, 1952, 1 patient out of 36 non selected admissions to two medical blocks at Newsham General Hospital suffered from malnutrition The total number of admissions to these two blocks was 792 The rather high incidence of 2 8% showing malnutrition is explained by the fact that the hospital admits mainly the higher age groups No comparable figures are available from other hospitals

Diagnosis of malnutrition was based on a detailed history supported by interview with relations or friends of the patients in the hospital, and with the help of the hospital almoner in the patient s home, and a clinical examination with full use of radiological and laboratory investigations, and in some cases with consideration of the response to specific remedies like ascorbic acid or high protein diet

An effort was made to obtain detailed information about the financial status of the patient and cost of the essential items of the weekly budget with special reference to food costs Old people almost all suffer from several disabilities, and in that sense malnutrition was rarely the only disorder Arteriosclerosis, hypertension, emphysema, and arthritis were often associated with it, but had no evident relation to the type of nutritional deficiency, nor did they materially affect any therapeutic measures taken Many more cases of nutritional deficiency were treated by us than the 39 under review, but investigations before 1951 were often incomplete and it was not until we introduced a special case record chart for nutritional deficiency that we obtained comparable data

Age-distribution

There were 18 men and 21 women in our review Their ages were

35–40	1	65–70
41–45	1	71–75
46–50	2	76–80
51–55	2	81–85
56–60	0	86–90
61–65	7	

The fact that 33 of the 39 patients were over of age is significant, even in a hospital which itself mainly with the aged One of us (H F lected cases of nutritional deficiency in another hospital of comparable size which admits all a and he has found the same prevalence of m in the elderly Only quite exceptionally was as a primary disorder, found in the middle or groups The social and economic history of gives the answer to the peculiar age-distribution industrial city the aged are financially the least group It is said that "the first cause of hu malnutrition is poverty," and in fact 29 patients series admitted lack of money as the main cause nutrition On closer analysis, however, it was just lack of money but unfavourable living c loneliness, and the inability to spend money which brought about the state of malnutrition causes of nutritional deficiency other than conditions were physical handicaps such as arthritis of hip-joints, Parkinson's disease, str diet, indifferent cooking, anorexia, and food but together they represent only a quarter cases under review It appears, therefore, pert deal with the financial and social aspects of ol some detail

Economic Factors

Various surveys in the past fifty years have the close relation between poverty and old between poverty and malnutrition The needs," or subsistence, as distinct from the diet and its weekly costs at current prices have calculated in those surveys (Rowntree 1918, 1934, McGonigle and Kirby 1936, Schulz 1948, If, as Schulz (1950) found, a single person could just obtain an adequate diet on about 12*s* per 1950 this must have been even more difficult in since the index for food prices increased from June, 1950, to 150 in January, 1952, thus rais figure of 12*s* to 14*s* 6*d* In the analysis of the of malnutrition in our group, we blamed poverty weekly budget provided 12*s* or less for food. The larity of the diet taken by these people was strik the following sample was typical

Breakfast —Bread and butter or margarine, tea

Midday (usually the main meal) —Either meat (m brawn) or fish or one egg, on about three days a week, p boiled or chipped, bread and butter or margarine At ends a vegetable and meat stew would take the place above midday meal

Tea —Bread and butter or margarine, jam and tea

Supper —Cocoa or tea

Most patients drew their full ration entitlement w exception of meat, which was often refused becaus expense, brawn being taken instead Green veget usually cabbage—were bought once a week Citr other fruit was rarely eaten

In 31 of the patients, details of income and expend were obtained, though accurate and complete f were not available in every case

Total expenditure on food for a whole family was k for instance, but it was not possible to assess how m spent on feeding the old man or woman within the f In a few cases food expenses were known, but not th weekly income In others details of fixed expenses (rent and fuel) were readily obtained, but the patients uncertain about expenditure on food In 8 patients income was between 25*s* and 30*s*, in 5 it was betwe and 35*s*, in 4 it was between 36*s* and 40*s*, and 4 patients more than 41*s* to spend Expenses for food were figures by 26 The average weekly sum spent on food 2s 2d The average rent was 7s 2d for 31 patients tients knew their fuel costs, with an average of 5s 2d r was the average for light and gas for 9 patients Only nitted relative extravagance on alcohol and cigarettes rently high to cut their resources for food below the num need Another 3 had to pay high rents, leaving too money for food

31 patients, 15 did not admit to any additional rces besides old-age pension The remainder ed supplementary pensions from the National ance Board, from private employers or in the form men s pension in addition to the old-age pension is much to be said for the view that primary ty among the aged can be avoided under present tions, but it does require an approach to the National ance Board—a step which many old people seem stpone as long as possible

Symptoms

tailed history taking in malnourished old people is ie-consuming and trying task which explains why utrition or even frank starvation often remains spected before admission of the patient to hospital as to be expected, malignant disease of the gastro inal tract figured first among the provisional oses given by the general practitioner Œdema iated with starvation was generally attributed to stive cardiac failure or nephritis, and massive ing into subcutaneous tissues from scurvy simulated itis. Only in 3 patients in our group of 39 had utrition been recognised before admission

e duration of subnormal feeding was difficult to Memory difficulties of the elderly were aggravated he apathy due to malnutrition and in many cases id to rely on the statements of relatives and friends period of deficient food intake before hospital treat- varied between two months and eleven years, with rgest group giving two years as the length of time feeding

e symptoms which led to the request for medical e in the first instance were varied.

orexia was the leading symptom in 10 patients d not prove to be a manifestation of starvation as us as it is in younger people (Schwarz 1915) vo out of every three patients complained mainly of *ude*—a symptom far too usual among the aged ill ve any special significance in malnutrition

ight loss was the leading feature in 24 cases but not reliance can be placed on this figure quite often got unsatisfactory replies about weight loss. No parable figures are available as to how younger le could have fared as regards weight loss on diet which rather older people had taken for so

imentary upsets in the form of constipation were ally mentioned by 12 patients but only 3 complained arrhœa—a proportion very different from that seen ne of us (Fuld 1945) in concentration-camp victims ig the late war The conditions of mass starvation mps however are entirely different from those of group and the absence of diarrhœa in all but 3 of cases was probably due to the lack of enteric tions which accompany overcrowding

of our patients specially mentioned *difficulty in owing* Of the 8 women 6 had a profound microcytic nia while the man had only a mild normocytic mia. Dysphagia is common in elderly women with utrition accompanied by microcytic anæmia of e degree; we presume that we were dealing with the mer Vinson syndrome

of our group mentioned *distressed breathing* as one heir main complaints. Uncomplicated starvation is not to cause dyspnœa even after some physical ise In 6 patients of our series the dyspnœa was to profound anæmia with hæmoglobin levels of and below; in others cardiac and pulmonary ficiency were responsible

Difficulty in walking was noticed by 22 patients and the causes included arthritis arteriosclerotic vertigo hæmarthrosis of knee joints due to scurvy intermittent claudication, non articular rheumatism ulcers of legs and neuritis. Most of these patients also complained of pain in the legs.

Signs

Severe emaciation was observed in only 3 of our female patients whose appearance was not unlike that of Belsen victims Their recovery was complete but took up to seven months

Less drastic *weight loss* was found in all but 11 patients of whom 7 were grossly œdematous so that the actual loss of body tissues was masked. Concealment of tissue loss by fluid retention is often observed in the course of obesity treatment.

Some degree of *œdema* was present in 20 cases; a third of these had cardiac insufficiency adequate to explain fluid retention on that basis alone Of the remainder 8 were grossly anæmic, and had scurvy or a low plasma protein Gross nutritional œdema affecting the whole body associated with ascites and pleural fluid such as was seen in concentration-camp victims was only observed in 1 of our male middle aged patients whose plasma protein on the third day of hospital stay was just over 5 g per 100 ml and who had lived on a diet free of water-soluble vitamins for several months Three injections of 100 mg vitamin B_1 on successive days caused a massive diuresis and completely cleared the fluid retention Patients with renal œdema were omitted from our list

Some degree of *vitamin A deficiency* would have been expected in our patients if one accepts the data of the commission of the League of Nations which in 1937 decided that an adult requires about 3000 international units of vitamin A daily This amount is present in about 3½ oz. margarine or 1¾ oz. butter or 2 pints of milk which is considerably more than the daily intake of most of our patients An adult only absorbs 25% of carotene from carrots or spinach—vegetables which were rarely taken by any of our patients. Xerophthalmia was not observed in our group No dark adaptation tests were carried out 12 patients showed hyperkeratosis of the outer aspects of thighs and legs, but in the absence of estimations of the plasma level of vitamin A we felt these changes could not with any certainty be attributed to vitamin A deficiency particularly as similar skin changes can be produced by deficiency of the vitamin B complex by vitamin-C deficiency and by senile atrophy of the skin

Only 1 of the patients under review to whom we have referred also showed clinical signs of *thiamine deficiency* The therapeutic dose with injection of vitamin B_1 at the onset of treatment when the patient had received no other form of therapy resulted in massive diuresis and cessation of diarrhœa

10 patients suffered from angular stomatitis or cheilosis There were in addition 13 who had glossitis alone 3 cases of long-standing diarrhœa and 1 male patient with diarrhœa and dementia which cleared up under treatment with compound vitamin B tablets. Almost all our patients were living on a diet grossly deficient of the chief sources of *vitamin B_2* particularly of fresh green leaves, liver kidney or pork

It is recognised that acute and complete starvation is rarely associated with vitamin deficiency Bruckner et al (1938) suggested that this is due to liberation of the required vitamins from tissue breakdown which would explain the experience that vitamin deficiencies are more prevalent in starvation not accompanied by severe weight loss Our patients suffered from semistarvation and it is in these cases that the type of food available determines the type of vitamin deficiency which is likely to develop The problem is difficult however as vitamin-deficiency symptoms such as keratomalacia follicular hyperkeratosis and œdema may be ascribed to the semi starvation itself rather than to a specific vitamin deficiency In doubtful cases we have been guided in the diagnosis by the effects of large doses of a specific vitamin given by injection We assumed for instance that disappearance of glossitis and angular stomatitis within a few days after intramuscular injections with large doses of the vitamin B complex can be of diagnostic value

The diagnosis of clinical *scurvy* was far less dubious than that of vitamin-B deficiency We saw 19 cases of scurvy, the clinical criteria being

1 History of gross dietary deficiency in fruit and fresh vegetables

2 Presence of hæmorrhages in skin, subcutaneous tissue, and joints, and swelling of the gums (absent in edentulous patients)

3 Positive Hess test

4 Significant results with ascorbic acid saturation tests (not carried out in all patients)

All but 2 of our scurvy patients were anæmic to a greater or lesser degree, 7 had a normocytic anæmia and the blood films of the other 9 showed microcytosis and hypochromia In 2 patients the anæmia was macrocytic on admission but became normocytic under treatment with ascorbic acid, as described by Parsons (1938) 17 patients developed scurvy because they could not afford vegetables and fruit One had adhered to a strict ulcer diet, and another was mentally deranged and unfit to cater for herself

We have not observed in our group a single case of malnutrition with clinical evidence of *vitamin-D deficiency* Nor have we seen the hunger osteopathy described in Holland after the Liberation

The *skin* of most of our patients was dry, loose, scaly, and atrophic—changes which recur in most reports from famines In our group with its high age-level no special significance has been attributed to these changes, which could be due to senile atrophy alone without malnutrition We were, however, struck with the high incidence of *pigmentation*, shown by more than a quarter of the patients This was general and not localised to the exposed parts One extreme case suggested Negro origin, which was not borne out by an interview with relations it was in fact a severe case of "melanodermia of vagabonds" in a heavily-infested starved woman whose home conditions were indescribable Some degree of skin pigmentation in most victims of starvation has been reported by one of us (Fuld 1945) from Belsen camp We believe that at least three factors were responsible for the pigmentation in our group—infestation, starvation, and possibly nicotinic-acid deficiency Pigmentation faded with improvement of the general condition

The *dental state* in 21 of our patients was deplorable, the remaining 18 were edentulous, dental caries was present in 14, the other 2 had pyorrhœa and loose teeth. It is often said that bad nutrition results in an increased incidence of dental caries, and that dietary improvement should reduce the tendency of teeth to decay There is no support for this view from field experiences during the late war, from reports from famine areas, or from controlled experiments The history of our patients suggested that their poor dental state was the effect of life-long neglect

Notes were made on the *mental state* of the 39 patients on admission to hospital The behaviour and outlook of 28 corresponded to the average expected in patients of their age-group and social environment, 11 showed definite changes, with apathy and an attitude of hopelessness in 9, and anxiety and agitation in 2 "Primary" senile dementia cases were omitted from this series The progress made during treatment, and the disappearance of mental aberration, suggested that the psychological changes were at least partly due to malnutrition, which had affected the whole organism including the mental functions

How far malnutrition as such can be blamed for mental changes cannot be assessed The relentlessly depressing effect of poverty, dirt and cold—but particularly of loneliness—over a period of years is in itself sufficient to cause personality changes, but it seemed to us that the profound state of apathy was a direct effect of malnutrition Some seriously ill patients in advanced states of semistarvation presented a typical appearance, identical with that seen among prisoners at the Belsen camp They lay curled up on their sides and were entirely unconcerned about activities in the ward, but often resented any interference, such as washing or examination Bladder and rectal incontinence almost invariably present during the first admission, and feeding was difficult at this often resented One may speculate about the of physical lesions in the central nervous system and resulting mental changes, but the tissue of the are more resistant to morphological changes than those of any other organs No post- examinations of the C N S were carried out in the few of our patients suffering from extreme who died within a few days after admission

Malnutrition and Gastric Secretion

Gastric secretion was tested in all our patients 3 who refused permission We were interested effects of malnutrition on gastric acidity and its to anæmia Our experience of normal or average of gastric acidity in the elderly was limited, since seldom arises for carrying out fractional test old people, except for the differential diagnosis of and for suspected malignant disease of the We have, however, records of fractional test a number of elderly patients who were clinically of digestive disorders, blood-diseases, and defects Of the 26 males above the age of six (58%) had a histamine-fast achlorhydria, while 42 females above that age, 26 (62%) had a absence of hydrochloric acid

In our malnutrition series 36 patients were fractional test meal within a few days of 27 (70%) had a histamine fast achlorhydria, 1 acid secretion, 5 showed excessive values for free hydrochloric acid, and 3 secreted normal Of these 36, 27 were re-examined by gastric at the end of their treatment At that time 7 patients initial achlorhydria had recovered their gastric 5 of them showing a normal acidity curve, 1 chlorhydria, and 1 hypochlorhydria The re after clinical recovery, still had achlorhydria. gained the impression that malnutrition contributes towards achlorhydria, and that treatment of malnutrition tends to restore secretion in some patients As a result, the inci achlorhydria in the recovered patients resembl which we found in our control series of people of the age group

Malnutrition and Anæmia

Apperley (1936) believed in a direct relation *red-cell count* of the blood *and gastric acidity* that a fall of the red cell count to half or two- normal is followed by disappearance of free hy acid in the gastric secretion He distinguishes between the achlorhydric anæmia of Witts and achlorhydria We could not confirm his obser 4 of our patients had a blood count of less than normal, but showed average gastric secretion in test-meals

All but 3 of our patients were anæmic to a varying from 80 to 25% hæmoglobin, with red as low as 2 million per c mm The anæmia was cytic in 12 patients, microcytic in 20, and macro Of the macrocytic anæmia cases, 2 had low protein on admission and had lived on tea, bread, jam After treatment, which included a high diet, but excluded folic acid, liver, and vitamin anæmia cleared up and the blood became Achlorhydria was converted into normal gastric in 1 of these cases

The third patient with macrocytic anæmia, aged admitted in a condition of extreme neglect She had several months on a diet which excluded any green veg on very rare occasions she took first-class protein in n or bacon Her anæmia was hyperchromic on admission million red cells, 60% hæmoglobin colour index 1 2) bone marrow count did not suggest pernicious anæmia nade a full recovery on a high protein diet reinforced by ins. This patient's condition was reviewed six and o months after her hospital treatment and although she recovered from her anæmia the colour index remained 1·0 On the last count she had 4 million red cells, 115% oglobin and colour index of 1 5

Treatment and its Effects

o treatment of complete and partial starvation in lderly did not present any special problems Only patients arrived at hospital in a state of starvation were that they could neither swallow nor digest le foods They were treated initially by skimmed drips through a Ryle's tube After two days on a régime they were able to swallow foods. The early bilitation diet was of low bulk in all patients, and lly consisted in skimmed milk reinforced by Casilan o) Compound vitamin B tablets 6 daily, with rbic acid 200 mg, were added There was rarely need for vitamin injections Iron was given orally ore often by intravenous injection In the great rity of our patients, simple foods taken by mouth all quantities frequently were well tolerated within or three days. Thereafter the nutritional rules which y to feeding in childhood were followed until such as the patients could digest and assimilate ordinary ital diet, distributed in four meals a day There no relation between gastric secretion and appetite r cases. Although most of them had achlorhydria he onset of treatment we found no indication for ribing hydrochloric acid. Given the chance most people tend to eat more than they need, and our nts ate surprisingly well after a very short period of bilitation. They kept on eating somewhat excessively after they had fully recovered

eight Gain—The value of gain in body weight is ult to assess. Fat deposits tend to increase at a r rate than that of active tissues, and changes in body ution are a complicating factor It is, nevertheless of the indices of nutritional rehabilitation Of 17 nts, 13 gained an average of 10 lb with a range of lb, 6 gaining more than 1 st Of the remainder 1 ved no change, and 3 lost an average of 4½ lb the er initial weight being due to fluid retention

he results in this series of 30 cases did not entirely esent our experience during the last seven years have treated a far larger number than the series rted here, but have omitted them because of lack ertain investigations or adequate follow up or on unt of associated diseases which had some major ence on the patient's condition. During the earlier s, at the time when the present wide range of biotics was not available we lost patients in an anced stage of starvation from sudden heart-failure from intercurrent infection In the present series lost only 1 patient, who developed an intractable rhœa

uration of Hospital Stay—The minimum time of for patients with nutritional deficiencies was three ks. Some advanced cases of starvation in the aged ired up to nine months for full rehabilitation Wide-ad pigmentation in long-standing cases of mal rition may take up to twelve months to clear More n than not hospital care had to be extended well ond the period required for physical recovery There o group of patients in whom social problems play a er part in the ætiology of the condition or in the isposal at the end of treatment. Many of them had homes to return to and neither relatives nor friends accept their care Some were eventually accommo-ed in municipal institutions and charitable homes re remained a group which refused to enter such itutions and therefore had to remain under the roof he hospital

Follow up

Patients were followed up after discharge either at the hospital or at home Specific questions were put to 12 patients, selected at random for visits in their homes by staff attached to the Medical Officer of Health's department in Liverpool We were interested to know whether the patients had seen their doctors (who had received full reports from us); and comparisons were made between diet after hospital discharge with the conditions before admission Details of the diet with supplements like vitamins and iron were recorded as accurately as possible Living conditions were compared with the pre hospital period and the investigator tried to find out from the patients whether they had in fact realised that under nourishment was the cause of their ill health.

The result of this small-scale inquiry was disappointing Of the 12 patients only 8 had visited their doctor at home or had called him in. Only 4 had improved on their diet and 2 more had kept well by taking vitamin C tablets for scurvy which was their original disability The living conditions of the 4 patients who were taking an adequate diet had materially improved.

CASE 1—Mrs. A, previously under the care of a landlady who is alleged to have given her short rations Now living with sister who looks after her well Her actual financial position is unchanged

CASE 2—Mrs B wife of a regular soldier living with 3 children She had been starving herself to feed the children and was admitted with an iron-deficiency anæmia (Hb 25%) She had been advised on diet by her own doctor and claimed to be eating more than before admission to hospital

CASE 3—Mr C lived alone in an old age pensioner's flat preparing his own meals. Now living with a son and daughter in law No actual change in financial position

CASE 4—Mrs D a widow still living with her son to whom the mother's condition was explained, and who had persuaded her to eat more No change in financial position.

All but 1 of the patients whose living conditions were improved had consulted their doctor Of the failures only 3 had visited their doctor since discharge. Adverse reports on personality and living conditions were made by the investigators in 5 of the 6 relapsed cases, of whom only 1 supplemented the deficient diet by vitamins and iron Of these 6 patients who had gone back to the sub normal standard of feeding 1 had returned to his common lodging house taking his meals outside (carbohydrates and tea) 1 refused any food containing fat and had lost 11 lb in weight since discharge and 1 had no cooking facilities except an open fire. In only 2 of the relapsed cases was lack of money the only factor

Prevention

Hospital treatment of malnutrition in the aged is long and expensive and—quite apart from humanitarian considerations—this should make us prefer prevention Inadequate feeding unsatisfactory housing loneliness, and hopelessness are the main factors which eventually bring the patients to hospital. Ideally they should have been dealt with at the source Yet only a small pro portion of people in this country know about the incidence of malnutrition in the elderly and its social implication

To quote David Lloyd George How we treat our old people is a crucial test of our national quality'

Care for the aged is, of course, primarily a family affair The duties involved, which usually fall upon a daughter or daughter in law are uncongenial. The problem is aggravated by the frequent necessity for the woman in the household to go out to work to supplement the family income For obvious reasons it is desirable that old people without a family should occupy the ground floor flats of tenement buildings or an old people's hostel in a housing estate with arrangements for com munal cooking and general supervision by a matron Until these ideal conditions prevail, we suggest that malnutrition and starvation cases be notified by the general practitioner to the medical officer of health, so that health visitors may investigate the social conditions of each case and report their findings to the hospital if admission is deemed necessary The health visitors should also be notified on the patient's discharge from hospital so that they can supervise him at home Iron tablets and vitamin compounds could be supplied to the elderly on the same principle as cod-liver oil is freely supplied to children

Lord Beveridge wrote "It is dangerous to be in any way lavish to old age until adequate provision has been assured for all other vital needs such as prevention of disease and the adequate nutrition of the young" But this was written in the pre penicillin days of 1942 when pneumonia still sealed the fate of many old people in the winter months of each year Since then changes in the age distribution of the population have been brought about to a great extent by the introduction of antibiotics, while adequate nutrition of the young has been assured and preventive measures against infectious disease in childhood had a great measure of success The conditions of Lord Beveridge's statement of ten years ago are therefore fulfilled, and the time has come to consider more closely the welfare of the aged population by directing preventive measures towards those over sixty These measures should include suitable housing accommodation for the lonely aged, arrangements for communal feeding and settlements for the aged, or "meals on wheels", vitamins and iron supplements through clinics, or through practitioners, to those in need, and regular visits by welfare workers to lonely elderly who have a record of medical attention for malnutrition

Summary

Even today, grave malnutrition in the elderly is not uncommon and often goes unrecognised.

A series of 39 cases seen at one hospital during seventeen months is described, with observations on the effect of starvation on the mental state in old age

The results of test meals in 36 of the patients suggested that malnutrition increases the incidence of achlorhydria in the aged In some cases, but not in others, the achlorhydria was reversed by treatment We have found no relation between achlorhydria and the degree of anæmia

Most of our patients had a microcytic or normocytic anæmia, only 3 had macrocytic anæmias

Response to treatment was generally good, but sometimes slow, and for social reasons the patients often had to be kept in hospital well beyond the period required for physical recovery After discharge from hospital many of the patients unfortunately returned to the diets or conditions which had caused them to starve

Prevention of malnutrition in the elderly will require combined action in the social and medical spheres For this reason notification of cases of starvation to the medical officer of health's department is suggested

We wish to thank Dr A B Semple, medical officer of health for Liverpool, and his staff for their coöperation in the follow up of our patients, and Dr J Carr Brundret, Dr F H Moorhouse, and Dr R Y Dawbarn for their ready help in pathological investigations and their advice

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INCISION FOR ACUTE APPEN

M R Ewing A K
M B Edin, F R C S, F R C S E M.D Camb
SENIOR LECTURER LECT

DEPARTMENT OF SURGERY, POSTGRADUATE ME
OF LONDON

The frequency with which the acute
approached, in this country, through a
paramedian incision must result from th
teaching in our medical schools of these a
choice They certainly have the sanction
the standard works on operative surgery
that these incisions should be discouraged in t
of the acutely inflamed appendix

The acute appendix has, of course, been
removed from the right iliac fossa through
incisions, ranging from the midline epigastri
groin incision for hernia This is no indicati
for their general adoption in the treatment o
which is responsible every year in Englan
for 1200 deaths as well as for a considerable

The ideal incision should give the most
to the appendix, with the minimum of
and retraction both of the parietes and of th
contents, it should involve the least openin
planes in the abdominal wall which may
sequent infection, for the difficult case,
safely extensible in either direction witho
nerves, it is helpful if drainage can be
established through it, it should be condu
rising without increased risk of hernia form
the risk of subsequent herniation should be
if a hernia does occur it should lend itself
sound repair

How do the incisions in common use fulfil th

INCISIONS IN RIGHT ILIAC FOSSA

The *muscle-splitting incision* gives a sligh
line of approach to the appendix, erring o
or flank aspect This is a good fault,
that it involves less disturbance to the gener
contents Not necessarily where McBurney
described it, but intelligently placed at
lower level according to the physical signs,
affords fair access If the exposure is limited,
can be safely extended laterally by cutting
oblique and transversus muscles, or mediall
the rectus sheath Being valvular it is quick
closed, is strong from the outset, and f
rising The risk of subsequent herniation is
should such a hernia occur it can be repai
excellent chance of success

The *muscle cutting incision* gives slightly
to the appendix with less retraction
bleeding ensues, however, it is more time-c
the making It lies parallel to the line of
nerves, which should therefore not be liabl
Whether they are in fact so immune in se
incision is a matter of opinion It has bee
that their inclusion in sutures during the cl
wound is responsible for the diffuse bulge
end of the scar which is seen from time to
incision is good for drainage and reasonab
early rising, the risk of hernia is not gre
results of repair are satisfactory

When appendicectomy is likely to be dif
an obese patient who has had previous att
diagnosed late, or when operating facilities an
are not perfect, a muscle cutting incision is to b
In so far as it cuts rather than separates
in the presence of likely infection it does
to the abdominal wall than does the mus

after *These disadvantages are, however in the* ult case more than outweighed by the better access h it affords, allowing the appendix to be removed less deep retraction, less handling of the bowel and peritoneal soiling

BATTLE S INCISION

eing placed closest to the surface marking of the of the appendix Battle s incision gives the most t access to it It is valvular and favourable for early lisation. On the other hand it opens up the rectus th widely involves considerable retraction, and ot be safely extended in either direction for fear njury to the 11th or 12th thoracic nerves In the ult case where extension of the incision has been ssary the risk of subsequent hernia is considerable uld such a hernia occur its repair is neither easy by any means always successful. In first describing incision for the removal of a non urgent appendix le (1895) stated that its advantage lay in the inter tion of the rectus muscle between the two parts of incision which would prevent the development of a a If drainage is used, the drain prevents this position of the rectus and therefore robs the incision s chief merit.

view of these disadvantages we maintain that le s incision has no place in the treatment of the e appendix

MIDLINE AND PARAMEDIAN INCISIONS

ese incisions have the support of tradition they have undoubted advantage in the treatment of the ult *pelvic appendix moreover* it is claimed for that if the diagnosis is incorrect, other lesions can ealt with conveniently through the same incision

s regards tradition the position should be carefully wed as regards other lesions such incisions ld not be used as a cloak for slovenly diagnosis, the excuse that the incision is the same in any The disadvantages of these incisions are formidable have hitherto been too little emphasised To the ndix in the right iliac fossa they give an oblique oach from the inner side across the general peritoneal ty *Handling and retraction of the lower ileum are* tial interfering with the natural process of locali on and favouring the development of immediate onitis and ileus as well as of subsequent adhesions. y rising is contra indicated because the abdominal cles in contracting pull away from the wound ly, but by no means least, the risk of incisional ia is probably greater than with any other abdominal sion. Further such a hernia is notoriously difficult ure and has not infrequently led to lifelong invalidism.

CASE RECORD

boy aged 10 years, was awoken at night by lower minal pain he vomited once When he was seen by octor next morning the pain had gone and he was n a bottle of medicine Four days later he was admitted ospital urgently with symptoms and signs of acute intesti obstruction including well marked ladder pattern visible stalsis Its cause was obscure

ration —After aspiration of the stomach and an intra us infusion the abdomen was opened through a right r paramedian incision Coils of distended ileum escaped the incision and after much retraction and handling he bowel foul smelling pus escaped from an abscess round ngrenous appendix lying over the brim of the pelvis on right side The appendix was removed and the wound d with drainage through its lower end Discharge inued for 2½ weeks, and the wound became infected. ncisional hernia developed throughout the length of the nd with 1¾ inches separation of the recti

admission.—Nine weeks later the patient was readmitted subacute intestinal obstruction a large tense coil of stine being palpable under the scar The condition did subside with medical treatment and laparotomy was *again necessary The boy is now left with a large incisional hernia He is a keen footballer and wishes to know when he may start playing again*

It was very much regretted that a muscle-splitting incision was not used in this case

CONCLUSIONS

In all cases in which acute appendicitis is diagnosed a muscle splitting incision should be made in the position suggested by the physical signs If removal of the appendix is difficult the incision should be prolonged by converting it into a muscle-cutting incision

If the diagnosis is uncertain but acute appendicitis is a possibility the first approach should be through a muscle-splitting incision. If the appendix proves to be the source of the trouble much has been gained. If the appendix is healthy and the cause of the condition cannot be readily dealt with from this approach a second incision is made in the appropriate place

A second incision may be an unpleasant surprise for the patient and is something of a blow to the surgeon s pride but it is of no significance when compared with the morbidity, both early and late which may follow the unwise removal of a gangrenous appendix through a median incision

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Medical Societies

MANCHESTER MEDICAL SOCIETY

Transfusion Problems

IN the section of pathology on Oct 14 Dr J F WILKINSON said that though the transfusion of blood and blood products often saved life it could also be wasteful unnecessary and even dangerous The decision to transfuse a patient and the type and quantity of the product to be used (whole blood, packed cells, blood fractions or substitutes) was the responsibility of the clinician, who alone could decide from a study of all the clinical and pathological features of the case

Dr F STRATTON, director of the North West Regional Blood Transfusion Service, observed that at the Manchester Royal Infirmary the reaction rate from transfusions was about 2 8% Assuming that the blood was correctly matched reactions were due to any of four factors pyrogens, which could be present in chemicals or arise from bacterial growth in distilled water too rapid transfusion ; the administration of small quantities of air which could be avoided by careful filling of the distal tubing of the giving set or sensitivity to plasma which was found in the recently delivered woman or where there had been abortion Such reactions could be avoided by giving *the blood slowly* in a carefully estimated amount by warming the patient (never the blood) and finally by a careful cross match, including a saline agglutination and Coombs test for incomplete antibody using a serum which was both potent and specific

Dr R F JENNISON speaking as a hospital pathologist responsible for the operation of a blood bank said that the refrigerator in which blood was kept must be locked only specified persons should be allowed to take blood from it all such removals being recorded and signed in a book. *The messenger taking blood to the wards should* produce a written slip to avoid mistakes in identity while any resident staff who were not attached to the pathology department and who might have to cross match blood at night should be examined by the pathologist to make sure that they were competent to make the necessary tests

Dr R W FAIRBROTHER said that some recent transfusion disasters had been due to gross carelessness

Clinicians often left the decision about transfusion to the most junior member of the team, and even to the sister in charge of the case During the past twelve months there had been two fatal accidents caused by nurses taking blood out of the refrigerator and connecting it up to the drip The surgeon should not ignore his responsibility in transfusion matters

Reviews of Books

Modern Treatment

A Guide for General Practice. Editors AUSTIN SMITH, M.D , editor of the *Journal of the American Medical Association* , PAUL L WERMER, M D , secretary, committee on research, American Medical Association London Cassell 1953 Pp 1146 £7 7s

THIS important book carries the weight of authority of 58 American authors of high standing, and is clearly the result of much labour and care Whether it will in fact, as the editors hope, provide a new kind of aid for general practice is less certain How best to provide help in a rapidly changing therapeutic era is still an open question and this book has not necessarily found the ideal method For the practitioner clear and precise advice is often needed , yet in many forms of treatment this is just what it may be impossible to give General principles may not be enough, and to omit some subjects or aspects of a problem because they are not solved or are still under investigation is more cautious than helpful

Nonetheless the book provides a vast amount of shrewd, balanced, and helpful information It is surprisingly up to date and for the most part simple and easy to read It is much more than a mere index of therapeutic agents and methods it is almost a complete textbook of medicine in itself and includes much that is not directly concerned with treatment Thus ætiology and diagnosis are included and there are separate chapters on laboratory methods of investigation, diagnostic radiology, and such subjects as the general principles of infection, the patient-physician relationship, and clinical immunology The chapters on psychosomatic medicine and geriatrics are particularly good There are no illustrations but the printing is beautifully clear and it is easy to see why the book costs seven guineas

The Ship Captain's Medical Guide

19th ed Ministry of Transport Editor M T MORGAN, M.C , M D , medical officer of health, Port of London H.M Stationery Office 1953 Pp 337 21s

THE price and size of the new edition of this venerable publication, once a slim pocket volume, may induce some ancient mariners to list it as an added peril of the sea But for all that it is a magnificent compilation on art paper in royal octavo with well-chosen diagrams and illustrations, many in colour

The contents range from bug destruction to bubonic plague, from ant-bites to the Archbishop of Canterbury (p 299) The whole is a gallant attempt to present to a layman of proved intelligence a précis of the more practical parts of the six year medical curriculum Added to this are 104 pages on first-aid and 25 on general nursing The authors have made the book readable despite its intense compression, and even a specialist will learn something fresh from the 8 pages on malaria or from the section on the venereal diseases It is not their fault that the antibiotics section is already out of date, though even last year few of us would have advised a 28 day course of penicillin injections The absolute restriction of chloramphenicol to cases of suspected typhoid fever also seems strange There could be little risk and possibly great benefit in trying a short course of this drug in lethal conditions when penicillin has obviously failed True to form, the fashion in artificial respiration methods has again changed Official blessing is now given to the Holger Nielsen arm lift back pressure method and a 5 page appendix with illustrations describing the technique is cunningly housed in a special pocket together with a further 56 page brochure entitled Medical Scales

At a conservative estimate, this volume should provide bedside reading to the conscientious ship's master for at least three return voyages to Australia

Adrenal Cortex

Transactions of the Fourth Conference, Novembe Editor ELAINE P RALLI, M.D , associate medicine, New York University New York Macy, Jr , Foundation 1953 Pp 165 $4 00

THIS account of the latest Macy conference o adrenal cortex gives an impressive picture of the and complexity of contemporary research into significance of the adrenal cortical hormones in and disease

The preoccupation of the conference members with purely experimental work (mainly biological and emphasises how slender still is the pharmacological which the therapeutic applications of the adrenal stero Of the four main discussion topics only one—adrena in man—falls into the clinical category Two long are devoted to the concept of the " permissive actio adrenal corticoids, and to the mechanisms through adrenal cortex can produce qualitatively different Although the argument is well sustained, and the Professor Selye's exposition gives much pleasure reading, the general reader may find this difficult stuf perhaps unrewarding The most useful section is that existence and nature of the salt-retaining hormone (" cortin ") detected by the Middlesex Hospital workers recently crystallised by Professor Reichstein. Dr Vogt's account of this steroid, and the discussion will be helpful to many now attempting to keep advances in adrenal physiology

A Study of Hæmoglobin Values in New South

R J WALSH, BARBARA J ARNOLD, H O La MARGARET A COOTE, HELEN COTTER. National and Medical Research Council Special Report no 5 Canberra 1953 Pp 84

THIS monograph supplements the surveys of globin values carried out in this country, the and elsewhere The photoelectric instrument fully described, as are the precautions taken to accuracy The results, which are well set out generally similar to those obtained in other It is interesting to note that in New South Wales the public servants, bank officers, and shop as who have the reddest blood the Armed Forces sh lowest mean hæmoglobin of the occupational tested Values in pregnancy remind us of the fall in hæmoglobin—from a maximum average of 1 per 100 ml to a minimum average of 12 10 g the 28th and the 32nd week. Diurnal variati considered and found not to be very important, at 1 P.M tend to be a little lower than average. authors support the opinion that the ear is the site for taking blood, and the vein the best. The on variations in childhood are useful, and an inter diagram shows the total hæmoglobin in grammes to the body during the years of growth , in the most is added in the 14th year, in the female in th year

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Natural History of Infectious Disease (2nd Cambridge University Press 1953 Pp 356 22s 6 The second edition of Sir Macfarlane Burnet's book, already has achieved a unique place among works on in diseases, is relatively unchanged There are 40 more, some new illustrations, a new chapter on chemotherap some rewriting of some of the older chapters Considera great changes in the incidence of infection and in the practice it may seem surprising that more alteration been necessary thirteen years after the first edition, this is a book about the biology of infection, and much we rank as revolutionary—including the introduction antibiotics—is too recent for the full impact on disease to have been felt Control of vector borne and immunisation against such diseases as diphtheria yellow fever, have had much more rapid biological The author considers that the mid point of the 20th may come to be seen as the period when it became cl infectious diseases could be virtually eliminated The for the future, as he sees it, depends much more upo threat to use microbiology as a weapon of war tha Nature

THE LANCET

LONDON SATURDAY OCT 24 1953

Truth from Statistics

HE W H O *conference on medical statistics*, held ondon last week[1] differed from many other inter onal gatherings of this sort by arriving at a firm constructive conclusion the delegates acclaimed concept of national committees composed of rested people from government and medicine ed by a W H O central unit and refreshed by ılar international conferences The intention is these should act as a statistical conscience *ulating and training people to do fresh work* ing rid of useless routine tabulations and publi ıg the value of statistical research The means to end were the main topic of discussion

he conference crystallised the notion that sampling edures are often cheaper, quicker, and better than arently complete collections of vital-statistical ı In the technically advanced countries, where stration of births and deaths is essential to the oth *working of systems of social security*, this is ted completely and reliably In no country ever is the cause of death always recorded arately—the registered causes of death from more n one disorder in older people are particularly open question—and in some countries the certifying sician may be influenced by the legal and psycho al consequences of certifying certain causes This culty can be overcome by necropsy or other special uiry in a *small but representative sample* Then n, the results of a decennial census may be affected movements of people from job to job or place to o *and thus calls for repeated sampling surveys* he occupational and geographical distribution of population. Sampling may be valuable too, in lies of morbidity no regulations demanding the fication of all cases of even a few non infectious ases would be fully obeyed but much could be nt from detailed reports of a small random sample nterested general practitioners Likewise in the nically less advanced countries where registration births and deaths is incomplete trends in fertility mortality can be discerned from the carefully rded *experience of small areas chosen to represent* ections of the country in such areas the preva o of sickness of all kinds can best be ascertained n intensive studies by mobile medical survey teams eed, whatever the need sampling can give answers kly, accurately, and cheaply Although the cost subject may be higher than in a complete survey total cost measured in terms of useful information, much smaller, and if time is indeed money the ld tabulation from a sample survey represents a hor saving At first sight it would seem unrealistic use sampling methods to check the accuracy of a nplete registration, but when for example some % of disabling illnesses are assigned to no clearly defined cause *the only possible way to learn more* is to investigate a representative sample and to generalise from the results thus obtained

Without trained staff all this would be out of the question, and the conference made parallel recommendations on training The United Nations central statistical organisation is producing instruction manuals, and the exchange between different countries of coding details and other training material should *ensure accuracy and uniformity in classification* Furthermore, the epidemiological and statistical section of W H O is being encouraged to attune training methods to the public health requirements of member countries These and other measures, such as special courses and fellowships will help to meet the need for lay ' health statisticians ' and for medical specialists in preventive medicine to interpret and use the results obtained The main problem now *rests with our own profession* Unless *the general* practitioner is convinced that certification has a clearly useful object he is not going to give it the conscientious attention it demands he must see that the data he provides are used quickly and effectively by other medical men—locally nationally and internationally It is his interest that the national committees must strive to seize and sustain

Coarctation of the Aorta

ANATOMISTS have recognised aortic coarctation for two hundred years Yet less than thirty years ago a cardiologist declared that ' the diagnosis is rarely made during life "[1], and it was only after the publication in 1933 of accounts by LEWIS[2] and EVANS[3] that *this situation was changed* *Coarctation of the aorta* is a very serious abnormality A few patients with it reach old age but without surgical treatment many die in infancy and of those who reach the age of 17 more than half die before the age of 34 The remarkable advances in vascular surgery[4] have however entirely changed the outlook

The cause of the defect is unknown, but it has been found in embryos and is probably a true error of development unconnected with the closure of the ductus arteriosus Its prevalence is difficult to assess, but it must be lower than the necropsy figure of 1 in 2000, *and obviously it is higher than the 1 in 80,000* estimated from mass-radiography examinations A useful distinction may be made between (*a*) the so called infantile type, where the defect is usually severe (sometimes amounting to atresia of the aorta) and is often accompanied by other congenital defects in the cardiovascular system and elsewhere, and (*b*) the adult type where the narrowing is less severe With this type there is commonly no other serious abnormality, but in 25% of cases there is a bicuspid aortic valve, and the prevalence of berry aneurysms at the base of the brain is undoubtedly higher than the average In some cases, too the ductus arteriosus remains patent In the adult type the constriction *varies from an annular stenosis to a narrowed segment* several centimetres long The constriction is usually *just below the opening of the ductus* but *may* be at or above this level or occasionally in the lower dorsal[5] or abdominal aorta With the stenosis there is often kinking and distortion of the proximal aorta , this may involve the left subclavian artery, which may bulge laterally and make the radiographic appearance more confusing The aorta on both sides of the stenosis may be dilated , proximally the dilatation, sometimes aneurysmal, may be partly due to the associated hypertension, but below the stenosis this cannot be so, and no entirely satisfactory explanation has been found It is known, however, that the vessel walls near the coarctation may be defective and lacking in elastic tissue, and this may be connected with a lack of the stimulus normally provided by arterial pulsation The presence of a high resistance in so large an artery produces considerable changes in the circulation In patients who survive, the adjustment is remarkably successful, and the blood-flow in the lower limbs is usually quite normal The collateral circulation which develops takes much of the total flow , but although this is normally very free it has a higher resistance than the normal channels, and the drop in pressure across these resistances is offset by a rise in the proximal blood-pressure This in turn calls for a compensatory mechanism to moderate the flow through the upper half of the body, and in fact the forearm flows are normal The hypertension, however, usually contributes to the patient's death, which may be due to cardiac failure, subarachnoid hæmorrhage, or rupture of the heart or aorta but a few succumb to bacterial endarteritis, usually affecting the aorta just below the coarctation

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[1] See *Lancet* Oct 17 1953 p. 818

[1] King J T *Arch Intern Med* 1926 38 69
[2] Lewis T *Heart* 1933, 16 205
[3] Evans W *Quart J Med* 1933, 2 1
[4] See *Lancet* Sept 19 1953 p 601
[5] Brock R. C. Graham, A. J P *Guy's Hosp Rep* 1952 101 207

The diagnosis of coarctation, provided the condition is kept in mind, is usually simple The finding of a high blood-pressure, especially in a patient of good—or even superior—physique should lead to palpation of the femoral pulses, which are always diminished and often absent The femoral pulse, when present, is delayed, compared with the radial pulse, mainly owing to the slow rise in the pulse wave , the very slight lag occasioned by the longer collateral route is imperceptible[2] This diminution of the pulse wave, however, does not mean that the blood-pressure in the legs is very low

Direct measurement from the femoral artery shows that, though the pulse pressure is small, the mean pressure is lowered by no more than 10–15 mm Hg and always by much less than the reduction in systolic pressure, which may be 80–100 mm Hg This is because the pulse wave is heavily damped by the resistance of the collateral vessels and the distensibility of the distal aorta. The position is analogous to that in patients with a collateral circulation around a thrombosis of a large artery , EDHOLM et al[6] have found that in the affected limb the flows and pressures are relatively normal

The drop in pulse-pressure may silence the Korotkoff sounds, thus making it impossible to take the blood-pressure by the auscultatory method and reinforcing the mistaken impression that the leg pressures are very low Many other clinical signs of coarctation have been described, but though they may occasionally draw attention to the condition they add little or nothing to the certainty of the diagnosis Perhaps the most valuable of these additional signs is the presence of dilated collateral vessels over the back , but these are not always visible and are seldom definite in patients under the age of 10 years Occasionally murmurs are audible , but they are not usually a prominent feature and are certainly of no importance

Radiology plays little part in the d coarctation, since this can be so readily es clinical examination, but occasionally notching ribs may draw attention to the disorder The which are on the inferior margins of the ribs to the elongated and tortuous intercostal they participate in the collateral circulation ing blood from the shoulder-girdle and chest into the aorta (The first one or two ribs affected since their intercostal arteries arise subclavian artery—i e , above the coarctation many years this appearance has been pathognomonic of coarctation It is not ever, in every case, and is seldom distinct in under 10–12 years of age In a few cases no been seen in congenital cyanotic heart-disease, may also develop after a successful attempt to the pulmonary circulation by establishing adhesions[8] It is usually best seen in the and is clearest about 2–3 inches lateral to the It should not be sought along the necks of the these areas so often appear wavy The heart may be rounded or globular but is not usually enlarged, and if left ventricular enlargement nounced aortic reflux should be suspected The knuckle may be absent , but just as often there many “ aortic knuckles,” from shadows thrown kinked subclavian artery and by the dilatation aorta above and below the constriction The the coarctation is not easily displayed by plain graphy , but it may sometimes be demonstr lateral or oblique tomograms, or by careful tion with a barium swallow[9] Not infrequently appearances are complicated by the presence aneurysm above or below the constriction, or from the narrowed segment itself or from an costal artery Angiocardiography should alwa done before the patient is operated on, since this show the length and calibre of the narrowed se and the disposition of the great vessels Great ca is needed in interpreting the filling—or non fill aneurysms, for the degree of filling is not alw reliable indication of the flow[10] Adequate p may occasionally be obtained by intravenous inj but direct aortography[11] gives shadows of greater density and contrast, and this method always be used

Coarctation was first corrected surgically CRAFOORD[12] in 1944, when he resected the nar segment and did an end-to end anastomosis in year-old boy Simple resection is still the oper of choice , but in certain circumstances, as Gr has pointed out, end-to-end anastomosis m impossible, and then grafting with a length of aorta may be the only way of bridging the gap will think, with BROCK, that no-one should sta operation for coarctation unless he has a graft bag—it will not always be used The graft need be viable, as judged by tissue culture , it seems as a scaffold into which new intimal and itial coats can grow The best age for operation ot yet been decided On the one hand it seems grafts do not grow with the rest of the body, and d therefore not be inserted until the patient is full grown and has a fully developed collateral lation, while, on the other hand, degenerative ges may develop in the aorta and elsewhere during scence and thus increase the technical difficulties operation Furthermore any unnecessary delay desirable since coarctation is a constant threat to Up till now the supply of grafts has been very ed and the surgeon has often had to wait until s available, but the results of recent experiments erilisation and preservation of grafts have been encouraging,[4 14] and it may be possible soon to lish a graft bank. It is not yet known whether theoretical risks as shrinkage of the graft or, con ly of aneurysm formation will be encountered in ice but this uncertainty should not hinder work h has already provided brilliant short-term results *y may be fatal, and many surgeons can recall* nts who have died while their names were on the ing list

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[6] Edholm O G Howarth S Sharpey-Schafer, E P *Clin Sci* 1951 10 361

[7] Batchelder, P , Williams R. J *Radiology* 1945, 51,

[8] Barrett N R., Daley, R. *Brit med. J* 1949, i,

[9] Robbins L L , Wyman, S M *New Engl. J Med* 248 747

[10] *Lancet* 1953, i, 1082

[11] Jonsson G Broden B Karnell J *Acta Radiol*, suppl 89

[12] Crafoord C *J thorac. Surg* 1945 14, 347

[13] Gross R. E *Ann Surg* 1951, 134, 753

Vagaries of Intelligence

is widely believed that every child is served out *a limited* quantity of intelligence which—like the of him—can go on developing till it reaches the of its capacity, but which cannot otherwise be nded The mature intelligence is thus thought to a direct, possibly predictable, relation to the al ration issued by heredity, just as the size of a nese pith flower which has expanded in water nds on the original size of the bit of pith This tical and convenient assumption is backed by the lligence quotient (I.Q.), which is taken to remain hly stable throughout life Many have criticised reliability of tests for assessing the I.Q., and almost many have thrown doubts on the underlying mption but these have had less publicity On ther page, Mr A D B Clarke PH.D and Mrs M Clarke PH.D bring fresh evidence that the mption is untenable and a group of papers *ntly published strongly support their contention* t intelligence far from being a fixed quantity, may y considerably during a lifetime

r J Tizard, PH.D,[15] discussing criteria of mental normality, deals first with weaknesses in our hods of testing A child's performance in tests is no means constant from one test to another so n a group of children are tested and retested by a ndard method, such as the Binet test, though the *rage* I.Q. remains much the same, *individual* I.Q.s y vary considerably

hus in a test with a test retest correlation of 0·9 on nediate retesting and a standard deviation of 10 nts, one child out of every three who gained average res of 100 on the first test would on being retested, re above 107 or below 93 because of errors of asurement ; and one out of every ten children with rage scores of 100 would score above 112 or below 88 the second test.

An I.Q. of less than 70 is very widely accepted as dence of mental subnormality—sometimes on the lts of a single test It seems that one child in three who scored 80 at a first test might, at a second test, fall into the subnormal group Again, early revisions of the Binet test were believed to have a standard deviation of 12–13 points, and an I.Q. of 70 points thus fell about $2^1/_2$ *standard deviations below the* mean, and cut off 1% of the population On some recently devised tests however, the standard deviation is nearly twice as much, and an I.Q. of 70 falls just over one standard deviation below the mean and so cuts off 10% of the population Another difficulty is that the standard deviation sometimes varies for children of different ages

> Thus the 1937 revision of the Stanford Binet test has standard deviations varying from 13 points at the age of six to 20 points at the age of twelve and an I.Q. of 74 achieved by a six year-old on this test is thus equivalent *to an I.Q. of 60 achieved by a twelve-year-old.*

Tizard also points out that even if scales for measuring intelligence were absolutely reliable—in the sense that qualified observers would agree perfectly about each person's standing on the scale—it would still be impossible to predict infallibly the subsequent performance of those tested, for our present tests give only one point on a curve of growth and development and "the slope of the curve is not the same for all individuals" Many studies have been published about this fluctuation in performance He quotes the findings of *Honzik Macfarlane, and Allen*[16] that tests of two year olds predict performance at the age of five to an extent little better than chance and though prediction improves as the age of the child rises it is always hazardous

> In a given group of children the I.Q. changed, during the growing period of six to eighteen years by as much as 30 or more points for 9% of the group by 20 or more points for 33% and for 15 or more points for 60%; it changed less than 10 points for only 15% Thus for one out of every three children a prediction made at a six year-old test would be wrong by 20 points at the age of eighteen

As Clarke and Clarke say "it is clear that in the general population the concept of a rigidly constant I.Q. is contradicted by the facts, I.Q. constancy over long periods of time during the years of mental growth is the exception rather than the rule" Some findings *reported by Dr Nancy Bayley,[17] from the Institute* of Child Welfare at the University of California, bear on this

> A study was made of a group of adults of superior intelligence who were tested by a concept mastery test designed by members of the Terman gifted study group at Stanford and tested again twelve years later Changes in scores between the two testings were compared on the basis of scores in the final test sex age-group educational level occupational status and estimates of general success ; and some individuals in each of these classifications had improved their score over the first testing among them the two oldest people in the group—who, moreover scored higher in both tests than the group averages.

Whatever may finally prove to be the predictive accuracy of intelligence tests for adults those available for testing young infants even when they are carried out by an experienced and informed tester, certainly have none Prof Jean Walker Macfarlane, PH.D,[18] who has studied the value of such tests for predicting the performance of children who are to be

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[14] Hufnagel C. A., Eastcott H H G *Lancet* 1952 i, 531
5 *Bull. World Hlth Org* 1953 9 423
[16] *J exp Educ* 1948 17 309
[17] *New York Times* Sept. 6 1953.
[18] *Bull. World Hlth Org* 1953 9 409

adopted, also finds that the predictive value increases with the age of the child, thus for children aged nine years or over performance at eighteen can be predicted fairly accurately for six or seven out of ten—though this is too late for most would-be adopters But the fact is that the tests are influenced by many things besides the child's intelligence and its developmental curve—by his growth-rate, moods, physical well-being, freedom from anxiety, liking for the examiner, and willingness to cooperate in the test "Test performance," as MACFARLANE says, "measures the level of functioning, which indeed has as one of its elements intellectual capacity or potential" Perhaps the growing use of such tests is encouraging us to place too high a value on intelligence Many other factors go to make a useful man, as TIZARD puts it "Intellectual and temperamental qualities, for example, are not closely associated with each other, nor is school success necessarily a good predictor of occupational adjustment" Thus the performance of a brilliant man may be hindered or completely overthrown by his temperamental or emotional defects, while a duller man who is easy in himself and with others may far outstrip his achievement

We have no clear idea of the effects of education on intelligence, but it evidently has far more influence than the concept of the stable intelligence quotient suggests TIZARD quotes R S WOODWORTH as saying "radical differences in education can create substantial differences in intelligence, as far as intelligence is measured by our tests" Studies of normal children have shown, in some, consistent upward or downward trends in I Q over periods of years, some of the changes amounting to as much as 50 points, while mental defectives taken from a bad environment, and placed in a better, show a gain in intelligence, as measured by the I Q CLARKE and CLARKE, in their experiment with 59 mentally subnormal patients, illustrate this fact again, and in a further 11 cases they were able to show that a history of a bad or a good home probably has a predictive value for the child's future progress They ask whether such relatively spontaneous changes can perhaps be accelerated and improved Their findings are, at all events, a good argument against a too rigid segregation of patients according to mental level the introduction of a few brighter children into a ward of low-grade imbeciles can produce remarkable advances in some who have seemed incapable of improvement Incidentally, the proportion of feeble-minded children who grow up into essentially normal adults is always high—about half to three-quarters in most studies A study made over fifteen years of 206 adults who as children had been classified as mentally subnormal showed that over 80% were self-supporting, 80% were married, and 80% of these had children The number of children per family was slightly less than the national average, and their mean I Q was 95

Genetics has as yet no clear message for us on this difficult problem Prof L S PENROSE[19] points out that eye, hair, and skin colours, stature, length of life, personality, and mental ability are each dependent on more than one gene, and the same applies to abnormal behaviour traits such as the common psychoses, epilepsy, psychoneuroses, and mental deficiency Moreover, the definitions of such characters as insanity, criminality, and mental defect are largely social standards which vary enormously in cultures "It is very difficult," he says, "to the genetical from the environmental variation in these traits" Adoption pr experimental situation in which the effects of environment can be critically studied C are not safe in making predictions about the gence of children from the study of one or parents

SKODAK and SKEELS, quoted by MACFARLA 63 children raised in foster homes, and also the mothers Only 20% of the mothers, as against the children, had I Q s over 100, and of 12 moth I Q s below 70, one had a child with an I Q abov and all but one of the rest of the children had 70 In another study of 269 family groups co nearly 1000 people JONES and CONRAD found is a statistically significant relation between the gence of parents and children, so that a prediction made with confidence for two or three out of children This is certainly better than chance, not of much practical use, since it is presumably sible to know in advance to which two or three out ten it applies

Taking it all round it looks as though f differential birth-rate is causing a decline national intelligence are premature, being co too simple a spirit There is a great deal of done on the normal fluctuations of int different ages, under stress, and in different and emotional environments before this question can be debated in an informed way even turn out that intelligence is less like a water-flower than a balloon, which expands as stretched

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19 *Ibid*, p 417

Annotations

AFTER OPERATION

IN his Harveian oration to the Royal Colle Physicians last week Dr George Graham departed precedent by showing charts, and though his of the Value of Physiology in Medicine began wi past it ended well ahead of the ordinary hospital p of today

His main theme was the application of physi knowledge to the care of patients after operation particularly the need to meet deficiencies of pota The first step in the treatment of postoperative was taken, he said, when Sydney Ringer in discovered that the frog's heart could be kept ing with isotonic saline solution made up with water but not with distilled water ("Physicians expressed contempt for results that come from pithed frog, yet the frog has been of great value medicine") It is now known that the more seve operation, the more potassium leaves the muscles, and loss of potassium from tissues and blood may produce syndrome which Whipple in 1923 called pancreatic mia Symptoms and signs of potassium deficiency inc muscular weakness, abdominal distension, ileal cramps, nausea, vomiting, lethargy, apathy, and de sion, with characteristic electrocardiographic ch These effects can and should be prevented, in debili potassium deficient patients who are to undergo operations, by preoperative treatment But injudi postoperative administration of potassium can cause poisoning, and skilful steering is needed to the Charybdis of deficiency without running on to Scylla of excess Skill is required because the caused by excess, though not so clear-cut as those iency are by no means dissimilar thus weakness ie limbs betokens too little potassium while true ysis betokens too much—a situation resembling in diabetes where the patient in coma may be ring from either too little or too much insulin. The of poisoning is reduced by always administering se at the same time, and potassium should never iven in the first 24–30 hours after operation (when blood potassium level may be high) or at night s some senior person is at hand to interpret any ge in the patient's condition In fact Dr Graham ves that the proper application of physiological vledge to maintaining the electrolyte balance of any ut who has undergone a severe operation needs the efforts of the surgeon and a physician, both with iological instincts and a knowledge of cardiology and biochemist—besides the registrar the house surgeon well trained nurses On the principle if prevent why not prevented ? ' this challenge from a senior ician speaking from the seat of Harvey is one that ot be ignored

TUBELESS GASTRIC ANALYSIS

On many patients a fractional test meal[1] is rather rdeal even when expertly carried out and any ble method of gastric analysis that does not call he passage of a gastric tube must command attention l and his fellow workers[2][3] in 1950 devised an int tubeless technique for detecting achlorhydria depends on the power of the hydrogen cation) of the free hydrochloric acid of the gastric juice pH of 3 or less to displace the quininium cation +) from a quininium resin compound When compound is ingested the quinine hydrochloride ied is rapidly absorbed from the small intestine and dine is excreted in the urine within 15 minutes The ine can be rapidly and simply estimated by a simple hod based on its fluorescence in ultraviolet light

his method has been reported on favourably in U.S.A[4][5] and has been carefully studied in this ntry by Harkness and Durant[6] In 200 subjects the hod was compared with an alcohol or alcohol plus amine test meal Comparison was impossible in nstances—in 13 the alcohol test meal was unsatis ory and in 7 the quininium resin method failed failures of the alcohol test meal were the more erous, and the more difficult to correct since the fault in the patient's condition (gastric hæmorrhage sistent vomiting refusal to swallow the tube &c) tubeless analysis by contrast had 4 failures arising n nursing errors administration of the resin and ection of urine; and these tests were later repeated essfully In 3 patients, however difficulties in the trol of micturition made the test impossible An ellent measure of agreement was found between the methods in the assessment of achlorhydria It found that excretion of 27 mg or more of quinine icated the presence of free acid Even with achlor dria, some quininium is released from the resin ause other ions besides the hydrogen ion displace the inium These other ions include sodium and assium *which are normally present in the secretions* l, more important, aluminium calcium barium l, and kaolin—substances which are commonly uded in medicines for patients with gastric dis er or anæmia Anomalous results were obtained ess such medication was stopped at least two s before the test Twice a positive reading was ained in a patient with a partial gastrectomy in whom two alcohol plus histamine tests showed achlorhydria but this is really understandable because of the variable factor of regurgitation through the stoma of neutralising juices from the duodenum and jejunum Malach and Banks[4] found a good correlation in 9 patients who were studied after gastric resection A false negative result may be found when defective renal function impedes excretion of quinine and this invalidated the test in 3 cases of the series reported by Harkness and Durant In patients with peptic ulcer one would not expect complete agreement between the alcohol and quininium resin technique Watkinson and James[7] noted from 24 hour gastric analyses that free hydrochloric acid was detected in no less than 10 out of 12 patients who had achlorhydria according to the usual histamine tests In contrast however complete anacidity was found throughout the day in patients with addisonian anæmia.

A serious disadvantage of the tubeless gastric analysis is that it does not indicate the level of acid secretion—Harkness and Durant found no correlation between the levels of excretion and the amount of acid judged by the test-meal But this disadvantage might be overcome through studies on the rate of acid secretion As Avery Jones[8] has observed, this new test may be useful in the investigation of patients with suspected addisonian anæmia but it is unlikely to have any other serious indications. Even test meals have only a limited value in the investigation of dyspepsias, but in the diagnosis of carcinoma of the stomach the appearance of the gastric juice may provide a useful clue

'WITH A BLUSH RETIRE'

In one of his tales of the future Kipling made a woman remark, in the pride of her youth 'I'm only forty' By this stroke he indicated a complete reorientation to the question of age people in that coming time expected to live to round about a hundred We—their ancestors, in a manner of speaking—are perhaps making the first move towards their adjustment we are trying to accustom ourselves to an expectation of life, at birth of 66 for men and 71 for women and since this average is affected by the mortality at younger ages and especially the infant and neonatal mortality many of us are going to live a good deal longer than that Moreover since the forces tending to keep us alive are to a large extent the same as *those operating to keep us well, many of us will* feel fitter than did aged people in the past There is no escaping the truth however unpalatable that more can be expected of us than of our forefathers. In their first report, the National Advisory Committee on the Employment of Older Men and Women[9] make this point afresh recalling the good reasons we now have for believing that many men could go on working after 65 and most women after 60 and emphasising three excellent reasons why they should Greater length of life of course is one reason and the rising proportion of older people in the community is another; the third is the country's need of workers.

The committee found themselves handicapped however by lack of information in making estimates of the numbers who might postpone retirement given the opportunity for further work At present some 400 000 men aged 60–69 and some 2[illegible]0 000 over 70 are going on working These represent just under half the total number in the 60–69 age group and about a quarter of those over 70 Over 100 000 in the unoccupied group aged 60–69 are chronically sick and unable to work but that leaves a further 350 000 who might possibly return to work given encouragement We need to know what kinds of encouragement and the Ministry of Pensions and National Service are now inquiring into the reasons

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ee *Lancet*, July 11 1953, p 3

egal, H L, Miller, L L and Morton J J *Proc Soc exp Biol., N Y* 1950 74, 218

egal, H L, Young, H Y *Gastroenterology* 1950, 16, 380

alach M, Banks, B M *New Engl. J Med* 1952 247 880

ecker F J, Maslon M *Ibid* 1953, 249 65

arkness, J, Durant, J A *J clin Path.* 1953 6 178

[7] Watkinson G., James A H *Clin. Sci* 1951 10 255

[8] Avery Jones F See *Lancet* Oct. 10 1953, p 762

[9] London: H.M Stationery Office Cmd. 8963 1953 Pp 62. 2s

why people of pensionable age retire or stay at work It is possible, of course, to guess at some of them lack of the chance to continue, and a feeling of having done enough already, are two likely deterrents Many women do two jobs for part of their working lives—a paid job of some kind and the job of housekeeping for their families They probably accept with relief the chance to take a pension and do only one There are other difficulties about increments to pensions, which we reviewed fully last year[10]

A fixed retiring age is not common among manual workers, but is often applied to clerical and administrative workers, and has led to a widespread feeling that retirement at such an age is a right There is no medical reason to support the fixed retiring age, on the contrary Firms hesitate to change or vary the age, however, because of difficulties about promotion of junior staff The committee insist that it is time to review all these difficulties and get rid of some of them The criterion for employment should be ability, not age

They have studied more fully than has been done before the obstacles facing the older professional people who want to go on working These may be encountered long before retiring age a typical case is that of the officer leaving the Forces in his forties, who may apply in vain for post after post Employers are chary of appointing him, sometimes because there are actuarial difficulties about latecomers to pension schemes, sometimes because they are diffident about asking an older man to take lower pay than his qualifications seem to demand, or conversely fear that he may not be worth the pay appropriate to his age There are also traditional reasons—a custom of recruiting only school or college leavers, an ill-founded belief that older dogs cannot learn new tricks There is evidence that the middle aged and elderly are more adaptable and trainable than is commonly thought, and that they are more reliable and less accident-prone than the young The numbers in the professions who are adversely affected in this way are not perhaps great, but they represent a waste of ability and expensive training In general the committee urge that firms should modify their rules so as to be able to admit the occasional late entrant and to keep on the efficient older worker after he has reached what they earnestly request should now be called the *minimum* age of retirement

POLIOMYELITIS VACCINATION TRIALS

Six months ago we discussed[11] some preliminary trials of poliomyelitis vaccines At that time Salk[12] had reported the results of vaccinating 161 persons with inactivated vaccines prepared from tissue-culture virus These preliminary results were encouraging, there were no ill effects from the vaccination, and many of the volunteers developed antibody to all three types of poliomyelitis virus Recently, Salk[13] stated at a meeting of the American Academy of Pædiatrics that 637 children and adults have now been vaccinated with several experimental vaccines, and again the vaccines appear to be safe and capable of stimulating the production of antibodies After Salk's statement a spokesman of the National Foundation for Infantile Paralysis reported that ambitious plans were under way for testing the protective powers of poliomyelitis vaccines Trials are being planned for early in 1954 and it is expected that several hundred thousand children will be vaccinated

While it is encouraging to see rapid progress in this important work, many people will be disturbed at the huge scale of the projected trial It is possible that the risks of a trial of this kind are very small, but there has been little time or opportunity to find them out The production of a few hundred thousand doses of vaccine the growth of all three types of poliomyelitis tissue-cultures of monkey's kidney, and the virus then be inactivated by formaldehyde in such that they lose all infectivity but retain their potency, and the time available for these preparations seems short Moreover, a trial scale will be much publicised and the public will the vaccines to protect against paralytic polio and produce no ill effects If they do not justify these expectations, there is a risk that the view of poliomyelitis vaccination may be prej some time to come

SEX CHROMATIN AND HERMAPHRODI

The disorder in normal sex differentiation human embryo which leads to hermaphr unknown Both sex chromosomes and autosomes genes which influence gonadal differentiation, is uncertain whether the development of the sex organs in man is determined thereafter by the hormones of the fœtus, by its genic constitution, a combination of the two

In the absence of knowledge of its causat aphroditism has been classified on an anato taking into account the histological appearances gonads and the morphological anomalies of the and external sex organs The true hermaphrod whom both ovarian and testicular tissue are rare, but pseudohermaphroditism (classified as or "female" according to whether the gonads or ovaries) is not so uncommon, and its prevalence population has been estimated to be as high as 1000[1] The rearing of these infants, however, —and understandably—at variance with their sex Many of the more severe cases of female anomaly—which are usually associated with overactivity—are raised as boys, and intersex with purely feminine external genitalia are raised as girls Where the external anatomy is vocal sexuality, considerable difficulty in attribut may arise, and Williams[2] suggests that equivocal are best treated as boys

The shortcomings of present methods of class hermaphrodites have led Moore and his colleag to develop a method of determining sex which pendent of the morphology of the sex organs use of Painter's observation[6] that sex chrom show histologically a characteristic deep staining perty, they investigated the stained appearances nuclei in the cat Nerve cell nuclei were first observation because of their large size and clear and it was found that in stained material from the cat a distinctive chromatin mass near the nucleol visible with an oil immersion objective in a high tion of cells, but was rarely seen in the nuclei of male cats This sex difference was in the cell nuclei of the other tissues and of the cat, and also in a number of other m species, including man Moore et al suggest that "sex chromatin" is derived from the sex and that the fusion of the two heterochr X chromosomes in female cells gives rise to a deeply staining chromatin which is readily visible lack of distinguishable sex chromatin in the attributed to the small size of the Y chromosome XY combination resulting in a chromatin mass too to be recognisable as an intranuclear entity App observation to man these workers were able by ying stained sections of skin biopsy specimens to r correctly the sex of 70 normal people They tenta ly suggest that skin biopsies from intersex individuals indicate the dominant sex, and cite two such s in which the chromosomal sex tallied with the ure of the gonads Moore et al suggest that investiga of the nuclear sex chromatin in a series of known s of hermaphroditism may establish a relationship ween the type of intersex anomaly and the chromo al sex of the subject, and perhaps throw light on the logy of the condition At any rate as a diagnostic sure this ingenious method may prove of considerable ic especially in infants

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[10] *Lancet* 1952, ii 767
[11] *Ibid* 1953 i 777
[12] Salk, J E *J Amer med Ass* 1953 151 1081
[13] See *New York Times*, Oct. 10 and 11, 1953

[1] Young H H Genital Abnormalities Hermaphrodit Related Diseases Baltimore, 1937
[2] Williams, D I *Brit med J* 1952, i, 1264
[3] Moore K. L Graham, M. A, Barr M L *Surg Gyne* 1953, 96, 641
[4] Barr, M. L Bertram L F, Lindsay H A. *Anat Re* 107, 283
[5] Graham M A, Barr M L *Ibid*, 1952, 112, 709
[6] Painter, T S *Amer Nat* 1924, 58 506

ANOTHER NEW ANTIBIOTIC

VERY *wide range of organisms are attacked* by the biotics now in common use; and additions to the are valuable usually as a second line of attack when nisms have become resistant to the usual antibiotics latest addition is carbomycin

arbomycin is produced by a soil actinomycete *ptomyces halstedii*[1] It is a crystalline monobasic stance containing carbon hydrogen and nitrogen a molecular weight of about 860 It is sparingly ble in water although salts such as the hydrochloride sulphate are water-soluble The antibacterial ctrum of carbomycin closely resembles that of hromycin although against the majority of sensitive ins erythromycin is the more active weight for ght Both agents are active against gram positive ci and neisseria and to a lesser extent against strains æmophilus, but they are essentially inactive against coliform group[2,3] The pneumococcus and hæmolytic ptococcus are among the most sensitive bacteria in o while staphylococci (including those resistant to er antibiotics) and enterococci are slightly less so The vity of carbomycin against staphylococci resistant to er antibiotics indicates a possible use for the drug unfortunately these organisms readily become resistant arbomycin in vitro Furthermore, the development carbomycin resistance is accompanied by erythro cin resistance[3,4] There seems to be no cross stance however between carbomycin and penicillin, ptomycin chloramphenicol aureomycin, or oxy acycline (terramycin)[4]

eports of clinical trials of carbomycin are at present but preliminary results are not encouraging hough the pneumococcus is highly sensitive to this ibiotic in vitro the treatment of pneumococcal umonia with it gives very uncertain results. 31 cases e treated by Finland et al.,[5] who concluded that the ults were ' distinctly inferior to those observed with of the antimicrobial agents currently recommended use in these infections. Pneumococci disappeared idly from the sputum of only 3 patients they were l present in the sputum of the remainder for up to days from the start of carbomycin therapy Of 7 ients from whose blood pneumococci were isolated ore therapy 5 continued to yield positive cultures for to six days Clinically a good effect was con ared to have been obtained in only 6 patients Bunn l Cook[6] treated with carbomycin 8 patients with umococcal pneumonia. Of these 8 4 responded isfactorily and in another the condition cleared after weeks; while the remaining 3 were classed as clear treatment failures, bacteriologically and clinically ' Blood-cultures were still positive forty-eight hours after the start of therapy in 2 of these patients

If infections caused by highly sensitive organisms respond poorly to carbomycin, the hope of benefit in those caused by less sensitive bacteria such as *Staphylococcus aureus* is very small. Hewitt and Wood[4] treated 9 patients with *Staph aureus* infections (3 pneumonia, 2 bacterial endocarditis, 1 carbuncle 1 skin sepsis 2 urinary tract infections) The blood-culture of one patient with endocarditis became negative but after five days the patient died from cerebral embolism Carbomycin therapy also caused complete resolution of the abscesses of the patient with skin sepsis. No effect, however, was observed in any of the other 7 patients Similarly Finland et al[5] observed no change in a patient with staphylococcal empyema treated with carbomycin *or in a patient with staphylococcal pyelonephritis and* bacteriæmia Brief reports of the value of carbomycin in other bacterial infections are no more encouraging

It seems, then that carbomycin is unlikely to take an important place in the treatment of bacterial infections Clearly it should never be the first choice for serious infections since it might deprive the patient of an antibiotic known to be effective As a second choice, however for patients who fail to respond to the usual antibiotics, carbomycin may occasionally be of value

CEREBRAL ANGIOMA

INCREASING use of carotid angiography has focused attention on arteriovenous angiomas of the brain and the observations by Olivecrona and Riives[7] in Sweden, on the possibilities of operative removal of these lesions has made their recognition of more than academic importance *The common symptoms are epilepsy,* subarachnoid and intracerebral hæmorrhage focal cerebral signs, and headache Mackenzie[8] has studied in detail the early manifestations in fifty cases. Similar lesions are found around the mid brain[9] but he has confined his attention to supratentorial angiomas

Arteriovenous angiomas are congenital lesions; but, as Olivecrona has shown by angiograms repeated at an interval of ten years they may increase in size, while symptoms may also be exacerbated by complications such as hæmorrhage and possibly thrombosis. In Mackenzie's series the first symptom arose before the age of 30 in 70% of cases and during the first decade in 10% Although headache was a common early symptom it was usually epilepsy or an intracranial hæmorrhage that drew attention to the presence of a serious lesion Epilepsy was the presenting symptom in 16 patients, and *in all except 1 of these there were focal features in* some or all of the attacks these features were usually recognised by the patient in the early stages of the fit but in a few instances a witness's account was needed. In some of these patients there was transient hemiparesis or dysphasia after the fits and by the time they came under observation at hospital 11 had permanent focal signs In 15 patients the first indication of the lesion was an intracranial hæmorrhage usually this was both subarachnoid and intracerebral but in 3 cases it was apparently into the brain substance alone without leakage into the subarachnoid space With the almost routine use of carotid angiography in patients who have had a subarachnoid hæmorrhage arteriovenous angiomas have been identified as the source of bleeding in about 10% of cases.[10] The clinical sequence of subarachnoid hæmorrhage followed by epilepsy may occasionally arise from intracranial aneurysms but should suggest the possibility of an angioma the opposite sequence of epileptic attacks followed by a subarachnoid hæmorrhage is however extremely rare with aneurysms and is

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[10] Falconer M *Proc R Soc. Med.* 1952 45 299

highly suggestive of an angioma Severe headache without special characteristics was a common symptom in the Swedish cases , and Mackenzie noted it as the presenting feature in 12 of his 50 patients He found that in some patients it had some migrainous features , but in retrospect it could usually be differentiated from constitutional migraine since the unilateral headache tended always to be felt on the same side of the head (the side of the angioma), while commonly in migraine opposite sides of the head are involved in different attacks The most characteristic sign of a cerebral arteriovenous angioma is an intracranial bruit A bruit is occasionally heard over a highly vascular cerebral neoplasm or in patients with Paget's disease of the skull, but usually it indicates a vascular malformation The bruit may be faint and intermittent and at times is better heard over the eyeballs than over the skull Olivecrona recorded a bruit in only 25% of his first series of cases,[11] and did not regard it as a very important diagnostic sign In Mackenzie's patients a bruit was heard in 24 of the 48 patients in whom it was sought It was relatively less common in patients in whom an intracranial hæmorrhage had occurred, the probable reason being that the more *deeply situated angiomas tend to bleed* *In a suspicious* case careful and repeated auscultation of the skull and eyeballs is certainly worth while, but the absence of a bruit in no way excludes the diagnosis of angioma

Other physical signs are variable , sometimes motor and sensory hemiparesis or hemianopia are found, and such signs are especially common after an intracerebral hæmorrhage Olivecrona suggested that in the presence of these signs without a history of massive hæmorrhage the cause might be thrombosis or anoxæmia of cerebral tissue due to most of the relevant blood-supply being shunted through the angioma , while Mackenzie believes that small hæmorrhages may take place and destroy cerebral tissue The diagnosis is finally made by carotid angiography ; and surgical treatment must always be preceded by this investigation, which reveals the source of the angioma's blood-supply

MOTHERCRAFT TRAINING IN PRISONS

TRAINING in parentcraft begins at birth, for the adult's ideas on the way parents behave are inevitably grounded on the way his parents behaved to him Not a few of the mothers sentenced for neglecting their children, and sent to the new hostel at Birmingham Prison for a training course in mothercraft, argue that they were convicted for something no worse than their parents did to them—without being sent to prison for it This hostel has been in action now since February, 1952, and in their latest report[12] the Prison Commissioners are able to give a cautious account of the way it is working Situated inside the prison grounds, in a building which used to be officers' quarters, it can receive 12 women at a time These are sent from prisons all over the country, the only qualifications being that they should be of star class, able to fit well into hostel life, and with long-enough sentences for them to complete the course Sometimes not enough women convicted of neglecting their children have been available, and then vacancies in a course have been filled by other star women prisoners who can profit from it

The courses have been arranged by the Birmingham education authority, public health authority, and children's committee, and have to be very simply planned , for as the commissioners say, "although the home conditions that led to the charge were usually appalling, this was often the result not of poverty but of wasteful and unintelligent spending, bad housing, which readily induces slovenly habits, unhappy marital relationships, or the low mentality and poor physique of the They return, on discharge, to the conditions in have already failed , so the aim of their insu to teach them to use whatever cooking equipment have in their homes, and the elements of house- sewing, washing, and ironing Some cannot rea write, and so have to be encouraged to memorise instructions They are not particularly anxious they arrive, to learn anything The chaplain of prison, who gives a little account of these women, that the teachers are confronted with an "a degree " of ignorance and idleness but that the not unduly discouraged by this Most of these grew up in surroundings where overcrowding, and broken marriages were commonplaces standards have thus always been low , and as own children came they have accepted a pro decline, even in their own low standards In one all bedding and all furniture had been sold—or to the hire-purchase firm—until nothing and the family lived in the house on the floor with n in the way of furniture But the women r training, especially when they have once had the surprise of finding *that they too can do things* Nothing is a better tonic for the demoralised little success It is interesting that few of the reveal any real degree of poverty most of the could have maintained their families on a modest reasonable standard, and where there were many the family allowances, properly spent, would sufficed to feed them The difficulty lies in the of the parents to put first things first—sometimes in an unparental inability to put the children themselves The chaplain cites the cases of a without bedding or warm clothing and with arrears, where there was nevertheless a good set , another where the children were underfed the father and mother afforded a night out every day and a third where the mother's first charge on housekeeping money was 3*s* 7*d* a day for for herself Sometimes the father gave his wife small a proportion of his earnings for *housek* and in two cases he had been long out of work , the main the trouble was a complete inability to wisely The instructors have therefore taken pains to teach the women how to budget for spending Squalid housing presents a more diff problem, but the mothers are brought to rea that rooms, however bad and crowded, can be kept and probably warm Overcrowding is the worst of decent standards when the children have to on the floor because there is no room for a bed, dirt dirty habits are almost inevitable Drinking gambling seem to be far less potent causes of child ne than overcrowding they are pursued, but not recklessly among the English today

The real test of the mothers attending these co comes, of course, on their discharge. The Wom Voluntary Service are doing good work by a "friends" for those who want them, to stand by when they return home Even when they have for such a friend some of the women do not keep touch with her , and though it is too early to asses effects of the course, the W V S reports suggest some soon slip back into their old ways No d this is because their circumstances are still too for them , and the prison mothercraft course, it has given them a better idea of what to work for, naturally not been able to reconstruct their in a matter of a few weeks What they probably is the help of a family service unit for a few m whose members could work with them in their own h and teach them to build on the foundations which mothercraft course has so well and truly laid

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11 Bergstrand H Olivecrona H Tönnis W Gefässmissbildungen und Gefässgeschwulste des Gehirns Leipzig 1936

12 Report of the Commissioners of Prisons for the Year 1952 8948 H.M Stationery Office. 1953 Pp 198 6*s*

Reconstruction

BASIC GROUP PRACTICE

HOW IT CAN BE DONE*

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N two previous articles I suggested that basic group ctice might solve many of the problems of general ctice today and thus stabilise the National Health vice In the second article I set out some of the tical details on which the success or failure of this e of practice depend In this third article I propose discuss what it costs to start and run a basic group ctice and how this kind of practice can be developed hin the framework of the N H S

Finance

ly estimates of the capital costs and running expenses on a general knowledge of what this type of practice ts in places outside Great Britain adjusted to the ue of money in Britain today They are overestimates ier than underestimates I have based my calcu ons on the five-doctor group which is probably the t size Five doctor groups are of course not practicable rywhere in Britain but my figures can be scaled down groups of four three, and two doctors and for those king alone in rural isolation

hus I suggested that a five-doctor group should ploy 2 nurses 2 secretaries (1 acting as receptionist) 1 relief nurse-secretary For smaller groups the ie staff would be

Four-doctor groups	2 nurses and 2 secretaries
Three-doctor groups	2 nurses and 1 secretary
Two-doctor groups	1 nurse and 1 secretary

he equivalent of these in people who can interchange s or part time people who can work to a roster

he cost of converting dwelling or business premises a medical centre will vary with the local value of perty More often than not premises will be rented leased rather than bought outright Once a suitable lding has been found it can be radically adapted and medical centre equipped satisfactorily—bearing in d that much of the equipment will be contributed n the surgeries of the doctors of the group—at an ial cost of approximately £1000 per doctor or £5000 a five-doctor group If the centre is to be built from ground up, it will cost about £3000 per doctor or 000 for a five-doctor group

ho heaviest running expenses are staff salaries and t (*assuming that the property is not freehold*) The ual cost of salaries for a five-doctor group would be roximately :

2 nurses	£1000
1 secretary	£400
1 receptionist	£400
1 relief nurse-secretary	£300
	£2100

ent will vary but should not exceed £750 per annum any reasonable lease The other main expenses are

Car maintenance	£1000
Telephone	£150
Stationery	£200
Journals, study allowance society memberships &c.	£500
Gas and electricity	£200
Insurance	£150
Depreciation at 5% (considered as a £5000 investment)	£250
Contingency fund	£100
	£2550
Staff salaries	£2100
Rent	£750
Total	£5400

onsidering this against the gross income from a panel 2 500 (estimated at £1 per head) the running expenses about 42% of gross takings This makes no allowance for income from sources other than capitation fees or for mileage allowances for running cars The running expenses of comparable groups which I have studied in other places were within the range of 30–50% of gross takings

On this basis the net income to be distributed among *the doctors working in the group is £8000 or £1600* per doctor This figure should be a minimum net average and can of course be considerably higher

Framework Offered by N.H S

In its first five years the National Health Service has done little to stimulate the development of group practice Hopes were centred at first on the possibilities of ill defined and little understood health centres ; but these hopes have only been fulfilled in two or three places, and by now have lost their charm both for the general practitioner and for the Exchequer They are monuments to the local authorities and the outcome of a do nothing ' policy in regard to the main structure of general practice

The capitation system of payment and the tax concessions offered to the individual general practitioner are both strong deterrents to the development of group practice The capitation system subsidises quantity and penalises quality Attempts have been made to *adjust* the original capitation fee so as to equalise the remuneration of the small list and big list doctor But the basic evil of the capitation system remains According to elementary economics payment by salary would be more equitable but most doctors resist strongly any suggestion of remuneration by salary and this resistance has doubtless been strengthened by the generous provisions of the Danckwerts award

The general practitioner is given generous tax concessions. Allowances for practice expenses for his private home when the surgery is in the house and for his car, &c all make it advantageous for him to continue to practise alone as he does today on minimum actual expenses but maximum theoretical expenses

Whether we believe that the doctor receives too little or too much of direct remuneration or that his tax concessions are overgenerous or niggardly we must if we are honest admit that it is to his financial advantage to resist any change in the present administrative structure which might (*a*) reduce the maximum size of his list or (*b*) make possible a closer scrutiny of the expenses on which he claims tax concessions The present structure thus deters rather than encourages improvements in the organisation of general practice but since it is unlikely to be altered radically we must try to devise, within this framework means of stimulating instead of deterring better methods of practice

Inducements

The first essential is that national funds be made available to doctors who wish to form group practices The sum of £100 000 per year which has been set aside from the Danckwerts award is quite inadequate As the N H S is at present organised it is hopeless to expect many doctors themselves to raise capital to establish a group practice and present banking controls make it difficult even for the few who may wish to do so to find the money

The capital cost of a medical centre which I have given above, is as low as possible and an enlightened Ministry or Government, taking a long term view should look beyond this and aim at a construction (as distinct from a conversion) programme To encourage group practice and to develop medical centres throughout the country I suggest the following scale of grants

Size of group	*Capital grant*
Five-doctor	£10 000
Four-doctor	£7500
Three-doctor	£5000
Two-doctor	£2500
Single doctor (where no alternative is possible)	£1000

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e two previous articles appeared on July 4 and Sept 19

These grants, of course, must be tied to specific conditions, which will improve medical care, preserve professional autonomy, and yet permit the control necessary for spending public money Some such conditions as the following might be suitable

1 That groups will limit themselves to a maximum of 2500 patients per doctor
2 That an additional sum not less than half the capital grant will be contributed by the doctors—i e, every Government £1 will be matched by 10s from the group
3 The doctors will agree to
   (a) Give a twenty four hour service
   (b) Keep unit or family records on forms provided.
   (c) Make these records available for bona fide research
   (d) Allow medical auditing by regional specialists
   (e) Take a minimum of two weeks' leave for postgraduate study annually
4 All capitation fees will be paid to the group and not to member doctors
5 The group will enter into a legally drawn-up partnership agreeing that
   (a) A group leader shall be named
   (b) The minimum share of the most junior partner will be not less than £750 p a and he will have the right of resignation, may be dismissed, or given full term partnership status at the end of twelve months
   (c) An annual sum of not less than £100 per doctor will be set aside for postgraduate studies, medical society memberships, &c
   (d) The maximum amount of work permissible outside the group (defined in terms of time or earning) will be set out
   (e) All professional earnings from extra group sources will be pooled and distributed in terms of the partnership agreement

Provided these general conditions are met, the agreement would permit payments in various ways—e g, to the group leader for administrative responsibilities, or to a group member assuming special responsibilities for, say, obstetrics or research

In my earlier articles I discussed the reasons for all these proposals, except the proposal that the doctors should themselves contribute half the capital I have two reasons for proposing this To be a shareholder in an enterprise is often considered an incentive to strive for success Again, these contributions will relieve the strain on the Exchequer The doctor's share should revert to the Government (by purchase on retirement or death of the original group members), otherwise a form of sale of practices would be reintroduced

There are certain obvious objections to this, as to almost any other, plan for financing medical services For example, why should one generation of doctors bear the burden of financing, even in part, facilities for future generations? On the scheme suggested above this is in effect what would happen, and, unless some form of sale of practices is to be reintroduced, there seems to be no alternative Naturally the doctors who contribute funds to the construction of medical centres should receive a fair rate of interest on their money, which should be regarded by them and by the Government as any other national loan investment There is no reason at all why one generation of doctors should subsidise another

Perhaps, in these circumstances, the reintroduction of "sale of practices" would not be so bad, provided it was clearly established that it was sale of material facilities and not sale of "good will," as in the past However, there would be many complications to any such scheme For example, a medical centre built in 1953 would be more likely to depreciate than to appreciate by, say, 1963 (if the "good will" factor is excluded), and the doctor making the initial investment would find it difficult to recover his money, let alone enjoy a reasonable margin of profit on the capital he had had tied up for ten years It may, however, be possible to work out some satisfactory scheme along these lines and so perpetuate the private-enterprise element, which some consider a [illegible] to better work and greater effort

Another plan would be for a local authority the doctor members) to contribute half (or an fraction) of the capital, and this alternative would much to recommend it Thus for the price of W Down the London County Council could have some fifty basic centres housing 250 doctors and approximately 625,000 people The value of this of joint central and local government enterprise has proved by the results of the Hill Burton G Hospitals Act in the United States Against such enterprise in this country is the general mistrust of local authorities and his not al less fear of being dominated by them But, if this method of financing the centres could two branches of medical service

But maintenance costs as well as capital costs be instruments of policy It is not wise, in an to take maintenance costs into account, to capitation allowance, pay excessive salaries, or fee-for-service schedule which is impossible to The onus should not be on doctors, either indiv collectively, to limit their net incomes in order to the quality of the medical care they can offer would now suggest that the research-worker should left to buy his own equipment or the professor to the salary of his own teaching assistants? To would destroy the foundations of research and as it is at present undermining the foundations of practice At least the salaries of all medical should be met from national funds and all record material should be provided

I estimate the annual cost of salaries of the five-doctor group at £2100 With the addition record-keeping materials, a subsidy of, say, £2500 cover most of the running costs of the group would of course be free to engage additional staff. a subsidy would reduce the expenses of the group approximately a quarter of their gross takings, if maximum number of patients per doctor was fixed 2500, and would compensate for the drop in income this limitation would cause The maximum net per doctor, from capitation fees alone, would then about £2000

Once the arrangements for setting up the completed, the autonomy of the group would be sanct The Government's final administrative would end with the signing of the partnership agree

Cost to the Nation

For a population of 50 million people, in which doctor looked after 2500 patients, 4000 five doctor (or the equivalent in smaller groups) would be ne If all the general practitioners of the country decide join the scheme at one fell swoop, the central Gov would have to put down £40 million (£10,000 per cen The doctors would have also to be paid off for shares, amounting to £20 million, over the next or thirty years If these shares were held by authorities, they would not of course have to repurchased with central funds

However, it is much more probable that, even with inducements suggested, the rate of entry into practice would be slow It could be planned on, or regulated and budgeted for, an eight year period example This would mean £5 million in capital per annum for eight years

If a subsidy towards running costs of £2500 per per five doctor group were offered, and there was equal growth of groups over an eight-year period cost in the first year would be £1¼ million, rising by same amount each year to a total of £10 million.

When the scheme was in full operation, practitioner services (in terms of doctors' incom capitation fees—and direct subsidy to running co group practices) would cost £60 million per annum.

ns of the total N H S budget and the importance of a d general practitioner service this would not be proportionate.

Administrative Problems

'he biggest initial problem would be to set up satis ory machinery for approving grants Before any nts could be made, the Ministry of Health (or a fessional committee appointed by it) would first have approve the site premises (plans for conversion or struction) and partnership agreements This would d both central and regional bodies able to give sound ice on architecture legal aspects and organisation and ling

ll registered doctors must be eligible to enter a group ctice and apply for grants there could be none of the ding and choosing among doctors to which academic research bodies are inclined when they contemplate ficial developments along these lines

riority should be given to groups of the size most able for local conditions That is to say a five tor group should be given priority over a four-doctor *hree-doctor group in a densely populated urban area* not necessarily over a three-doctor or two doctor up in a village

fter a trial year a group which wanted to expand its nbership (up to a maximum of five) should be eligible an additional capital grant and staffing allowance up but not exceeding, the sum available for the larger up

nce minimum standards were agreed, the adminis ion of the scheme would be a big but not impossible k and one which would grow less with the years of the greatest initial difficulties would be to ourage doctors to form groups of a suitable size for re would be a natural tendency to try to form among nds groups of two or three rather than five As ucements five-doctor groups could be offered priority ger grants, and more staff

nce they have accepted the conditions set out above groups would be completely autonomous. The lical auditing of work within the groups would be le on a professional (as distinct from Ministerial) is, as it is in the better hospitals. Its purpose would not to police and discipline the weaker brethren but advise and help them

he personal or family record card (supplied by the istry) should be standardised so that it could be used research *But it should be designed by general* ctitioners to meet the needs of general practitioners, l not by Ministry officials whose chief interest is ninistrative ease and technique

General Comments

he financial and administrative programme I have lined is revolutionary But it is a revolution which ld take place within the present framework of the H.S It does not disturb established *traditions*—e.g capitation method of payment—and it would remove ny of the more reasonable and substantial worries of eral practitioners Capital needed would be no ater than the sum conceded to general practitioners retrospective payment by the Danckwerts award.

scheme of this kind calls for a more flexible attitude administration It calls for a renunciation of the gue dreams of 1948 of health centres as a possible ans of integrating the preventive and curative services l at the same time compensating local authorities for ir hospitals. But more than anything else it means ting the patient first, above and beyond any con erations of administration or concessions to the tors in the name of political harmony

n the positive side, from where the doctor sits, basic mp practice offers the general practitioner the chance to regain his prestige by improving his performance and the opportunity to become in reality all he is supposed to be in theory

The hard headed financial expert might well ask what can it offer in saving of cash apart from the invaluable but intangible benefits of improving general practice ? It is impossible to give a clear-cut answer to this question but two points are worth considering :

(a) *The better general practice becomes, the less work* will fall on the hospitals, where the care of patients is most expensive

(b) A large proportion of N H.S. expenditure is for drugs and medicines Overprescribing is an index of unsatisfactory medical care particularly at the level of general practice, and there is no administrative way of controlling this properly Even the largest American voluntary insurance schemes with rigid administrative controls and limited scope, cannot afford to offer drug benefits. The man who signs the prescription and no-one else regulates the size of the drug bill of the nation Better methods of general practice particularly methods which allow the doctor more time to be with his patients, would probably reduce the rate of prescribing

I believe that the saving in the drug bill which would follow the introduction of basic group practice would more than meet the cost of the capital grants and subsidies offered under the scheme

Again without group practice and all that it implies general practice research can never return the dividends of which it is capable

In the narrow sense, the N H S is no longer a political issue It is accepted by the people and by all political parties It is from the doctors that the lead must now come, and it is to be hoped that the new College of General *Practitioners and other professional organisations will* outgrow their fear of mixing politics with medicine and recognise that medical economics and organisation are the instruments of policy and mean more than the size of doctors incomes and the capitation fee The finance and the organisation of general practice are now the politics of medicine in Great Britain

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Special Articles

HOW CONSTANT IS THE I Q ?

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Since the early years of this century intelligence tests have been used as measures of general intellectual capacity and an immense body of published work has grown up around the subject Nowadays the intelligence quotient (I Q) is widely employed in educational selec tion and clinical procedures and there is no doubt that *intelligence tests provide* a method more valid than subjective or clinical judgment in assessing a person s intellectual level Not only is the I Q used as an estimate of a person's present intellectual status but the addi tional assumption has developed that this remains sufficiently constant during the life of the individual for fairly accurate predictions to be made about his future ability In other words, a person s intelligence at for example the age of 5 would be the same relative to others of his age-group at later ages ; thus the young genius would always be a genius the average child would always be average, and the defective would remain defective Such are the implications of a belief in a constant I Q a belief which within broad limits seems to be in accord with common observation Nevertheless, how broad such limits may be is of great importance at present when the I Q is so widely used in selection (e g , of school-children at the age of 11), and in this paper we consider this point

Mental Growth in Normal People

In the United States there have been many studies of I Q constancy which have as yet received little publicity in this country It is not our aim to provide a comprehensive bibliography, but the few references given will enable the interested reader to trace several hundred researches bearing on the problem

Nemzek (1933) and Thorndike (1940) summarise in all 359 studies carried out before 1940, and such researches show consistently that (*a*) the predictive value of the I Q (as measured by test retest correlation) decreases as the interval between the tests lengthens, and, as a corollary, (*b*) although the group or population average may not alter greatly, there will be considerable change of status of some individuals within that group (subsequent retests showing that to varying extents some subjects increase in I Q, some decrease, and some remain constant), and (*c*) mental tests given to children during the preschool years have usually little predictive value, and that assessments during infancy have no relationship with later status (except of course in such clear cut clinical entities as mongolism, microcephaly, and the like)

To illustrate the first two conclusions, the practical implications of commonly observed test-retest correlations may be considered Reviews by Nemzek (1933), Thorndike (1933), and Thorndike (1940) have shown that retest correlations are rarely as high as 0 95, and that on *immediate* retest the most probable value is 0 9

Shapiro (1951) demonstrates the implications of this second finding as follows "Let us assume that we have a test with a test-retest correlation of 0 9 and a standard deviation of 16 These data mean that, out of every 3 children obtaining an average score of 100, one would obtain a retest score above 107 or below 93 On the basis of the same data, out of every 10 children obtaining an average score on the first test, one child would obtain a score above 112 or below 88 on the second test (These illustrations assume that no learning has taken place)"

I Q changes may, of course, occur for a number of reasons errors of measurement as well as genuine alterations in the rate of intellectual growth may account jointly or separately for lack of perfect reliability

Over time-intervals of several years, test retest correlations are usually much lower than 0 9 Honzik et al (1948) found a retest correlation of about 0 6 for a time interval of 12 years, after following up a representative sample of urban children from infancy to the age of 18 years

They tested over 150 children at the ages of 6 and 18, and found that the I Q s of 58% changed 15 or more points, the I Q s of 35% changed 20 or more points, and the I Q s of 9% changed 30 or more points In only 15% of cases was the change 9 points or less Individual I Q constancy over this period was thus the exception rather than the rule The group averages, on the other hand, showed a maximum shift in I Q, over this period, of only 5 points The maximum I Q change for any individual was 50 points Similarly, Hilden (1949) who is in process of studying the intellectual growth of 100 children, has reported findings on 30 of these examined from early childhood to late adolescence In this small sample, too, individual variability in I Q was often found

Dearborn and Rothney (1941) have reported findings from the important Harvard Growth Study in which both mental and physical development in children were investigated over many years, their book gives results from many different researches on several hundred children They conclude that "prediction of growth at various ages is extremely hazardous, but is particularly so during the period of adolescence marked variability in individual growth curves appear throughout the course of the growth period The principle of individual variability goes right to the root of such problems as constancy of the I Q We have established the fact that variability rather than consistency of growth is the rule, that prediction except for average of groups is extremely hazardous "

To illustrate conclusion (*c*), namely that in the preschool years have little predi Honzik et al can again be cited

Tests at 21 months correlate less than 0 1 with at the age of 18 years Similarly, Bayley (1940) mental scores derived from tests at 7, 8, and 9 correlating highly with scores a few months later, relationship in the region of zero with all after the age of 30 months Indeed, in at least three quoted by Jones (1946), small negative correlations found between intelligence scores in infancy and test in later life As age increases, however, so does the with later intellectual status Thus, Bayley (1949) that for 27 children tested from infancy onwards, the tions with the test score at the age of 18 years positive from the age of 2, and by the age of 4 had 0 52

From the wealth of available data it is clear the general population, the concept of a rigidly I Q is contradicted by the facts, I Q constancy long periods of time during the years of mental is the exception rather than the rule Moreover, conclusion is based on the findings of researches in individual rather than group tests were used most part, all that has been said applies with greater force to group tests (widely used for which are in general less satisfactory than intelligence tests

Intellectual Changes in Mental Defectives

The general thesis advanced above can be illustrated by some work we have done recen mental defectives This has led us to ask permanent is intellectual subnormality? Is defective, always a defective' true?"

In the past there have been several studies exclusively of feeble-minded, non-organic d which I Q changes—often large—have been Such writers as Burt (1947), McKay (1942), (1945), Spaulding (1946), Sarason (1949), and (1949) have described I Q increments, some as 43 points These investigators, however, while various hypothetical explanations for the chan intellectual level which they demonstrate, rarely submit their hypotheses to experimental proof same criticism can be applied to the studies of already quoted.

We have retested with the Wechsler test over 100 adolescent and adult certified de The population from which they were drawn has been described by MacMahon (1952) As a routine intelligence testing we observed that patients who had been examined a year or more with the same test showed large I Q increments, we planned a research to elucidate these I Q and to determine the frequency of their occurrence

The main experiment entailed the retesting of 59 subjects after an average of 27 months had elapsed the original test, 27 of these patients increased their by 8 points or more, 17 by 10 points or more, and points or more, the maximum increment being 25 The remaining 32 patients showed small increases or Increments were general throughout the sub-tests Wechsler intelligence scale, and were not merely conf a few of these The test-retest correlation was 0·90

In order to determine the maximal effect of test tice, errors of measurement, and underestimation at time of the first test (since many certified feeble-m patients are emotionally unstable their intelligence occasionally be underestimated when they are a control group of 29 mentally subnormal mostly new admissions to the Manor Hospital hed with the main group for initial I Q and age was retested after a short time interval (average aths)

---

* This study has already been reported to meetings of the Deficiency Section of the Royal Medico Psychological tion (Nov 5 1952) and of the British Psychological (April 13 1953)

retest these subjects showed an average increase of ats, the majority showing changes between plus and 4 points only 6 had increments of 8 points or more aly 1 of these had an increment of over 10 points (13) The distribution of these changes may be seen in I The control group data, therefore indicate that the o increment of 4 points upon retest represents the o maximal effect of test practice *errors of measurement*, itial underestimation In terms of test retest correla 0·94—the reliability of the test is quite high on this ation

ral hypotheses were advanced to account for the se in I Q shown by the members of the main group of these hypotheses was critically examined, but cases but one the evidence was such that they o be rejected The exception was that there was ng relationship between very adverse early home tions and subsequent I Q increases Twelve clearly d criteria of adverse home conditions were formu —N.S.P C C intervention orders appointing some- a 'fit person'' to have charge of the child, parental de antagonistic towards the child home conditions bad home dirty and neglected child considerably ted, no fixed abode irregular school attendance due rental neglect, gross poverty deficiency diseases, found begging or wandering and parents or sibs minal records. These were applied to the 59 case ies under consideration, and the presence of two ore of these somewhat overlapping criteria was as clearly indicating very bad home circumstances s found that those who had been subjected to such se early environments were mainly those who made I Q increases. An external investigator (Dr J Tizard Medical Research Council s Unit for Research in ational Adaptation) who had no knowledge of either atients or their test-scores, independently analysed ase histories he agreed with our assessments of conditions in 55 of the 59 cases in the remaining es his rating was accepted as final Evidence of bad home conditions was found in 25 case histories in the remaining 34 there was either no evidence lly adverse conditions or a complete lack of data ling early home life, or (in only 6 cases) clear nce of a good home Tables I and II show the results of the investigation

difference between the gains made by the ' very home'' group and the remainder is significant d the 0·1% level which shows very clearly the association between early adverse environment Q increase many years later It is consistent with nding to suggest that the environment which is *antagonistic towards the child* retards mental opment for many years. Later however after al from such conditions this retardation begins le and I Q increments occur often at ages when l growth is commonly assumed to have ceased

rospective validation such as has been described with it the possibility of error as a result of e relationships in the records of those investigated. s necessary therefore to ascertain whether the criteria of bad homes were equally effective in predicting I Q changes as they had been in discriminating retrospectively

TABLE I—DISTRIBUTION OF I Q CHANGES

ange (points)	Very bad homes (25 cases)		Remainder (34 cases)		Control group (29 cases)	
	No.	%	No	%	No	%
o 6	1	4 } 100	8	24 } 100	4	14 } 100
o + 7	6	24	17	50	19	66
r more	18	72	9	26	6	21
r more	12	48	5	15	1	3
r more	7	28	0		0	
	1	4	0		0	

TABLE II—CHANGES BETWEEN TEST AND RETEST IN FULL SCALE I Q POINTS

—	Very bad homes (25 cases)	Remainder (34 cases)	Total group (59 cases)
Mean change	+ 9·7	+ 4·1	+ 6·5
Standard deviation	6·3	4·9	6·2

t = 3·86 significant beyond 0·1% level
I Q range at first test = 36–98 mean = 66·2; S.D = 11
I Q range at retest = 49–97 mean = 72·7 S.D = 12·4
Age range at retest = 14–50 years mean = 23·5; S.D = 8·1 years. (Only 9 patients were aged over 30.)
Period between test and retest: mean = 26·0 months S.D = 6 *months*
Range of I.Q changes − 7 to + 25 I.Q points.

There remained at the hospital only about 20 *patients* who had been tested two years before and who had not already been retested for the various experiments included in the research from these 6 cases were selected whose records clearly indicated adverse home conditions, and *a further 6 were found who had come from homes which seemed* unlikely to have been very bad. Increments were predicted in *the former* but not in the *latter* and it was only after definite predictions had been made that retests were undertaken The changes in I Q points for those for whom increments had been predicted were + 14 + 9 + 10 + 10 + 4 + 5 average + 8·7 points the changes for those for whom *increments were not predicted were:* − 5 − 2, + 7 − 1 + 4 average + 0·6.

It will be noted that on this very small group the criteria show some predictive value it would, of course, be desirable that this finding should be checked on a larger group and indepedently as was the retrospective validation

The I Q changes in this investigation were largely in the upward direction whereas in some researches already quoted the variability was equal in both directions This, however is probably the effect of the very adverse backgrounds of the certified feeble minded and it is not suggested that the factor shown to be associated with I.Q changes in this research is necessarily the only one underlying changes in general Other investigators have suggested both this factor and others in relation to the problem of I Q inconstancy As already noted however these hypotheses seem never to be carried to the stage of experimental validation

The results show clearly that intellectual retardation among such deprived people as have been studied here is not necessarily a permanent and irreversible condition Obviously too the increases demonstrated over a period of two years will not represent, in most cases the total change which the invididual has already made or will make in the future As Honzik et al. (1949) point out some subjects show consistent trends in I Q changes over a long period

Conclusions

It is evident from the work of many different investigators that, group averages apart, considerable changes in intellectual level may take place during the course of individual development and that the question is not so much Is the I Q constant ? but rather How constant is it ? As Honzik et al. put it

> Whereas the results for the groups suggest mental test stability between 6 and 18 years, the observed fluctuations in the scores of individual children indicate the need for the utmost caution in the predictive use of a single test-score or even two such scores This finding seems to be of special importance since many plans for individual children are made by schools juvenile courts, and mental hygiene clinics on the basis of a single mental test score "

The fact that all longitudinal studies of intellectual growth show a decline in predictive ability of the I Q with increase of time implies change in individuals

The I Q, percentile grade, or standard score must be regarded as an objective estimate of a person's present intellectual status, and it is certainly better (even for predictive purposes) than subjective judgment or unstandardised examinations When we use the I Q for prediction, however, we must realise that errors are inevitable, and that these errors may have far-reaching and serious consequences for individuals selected by the tests for particular purposes

The fact of I Q variability can no longer be disputed, and the evidence is rich in implications Let us consider merely one example it has been shown that a group of socially deprived, mentally subnormal people tend, when removed from adverse conditions, to advance towards intellectual normality Can such relatively spontaneous changes be accelerated and improved? These and many other related problems invite the psychological and psychiatric investigator to a clear field for research

We wish to thank Dr J F MacMahon, physician superintendent of the Manor Hospital, for his help and encouragement during this research, Mr M B Shapiro, senior lecturer, in the psychology department of the Maudsley Hospital, for stimulating suggestions and criticisms, Dr J Tizard for help in an essential part of the experiment, Mr A Ehrenberg, of the statistical laboratory of the Maudsley Hospital, for useful advice, and Mr G J F Singleton for the statistical computations

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SPECIALISATION AT SIXTEEN

SPEAKING at the inauguration of the new session at Westminster Medical School on Oct 12, Mr H E Harding, F R C S, the dean, spoke strongly of the effect of the changed requirements for matriculation at London University

"In the past," he said, "a student matriculated at about 16 years with credit passes in a minimum of five subjects and thereafter spent two years working for a Higher Certificate in subjects of his choice and aptitude, knowing that he had a place for medicine The new requirements are six ordinary-level passes and at a subsequent examination two advanced level passes The results of these examinations are available in most cases only a week or two before entry to the University course and our final entries cannot be determined until this date We have been very concerned that some of the best candidates on general grounds have failed to satisfy these requirements and a last-minute revision of acceptances has been necessary Not a single applicant offered advanced level subjects in English language or literature—in fact most had become scientific specialists from the age of 16 This drift from the humanities, our language and our literature, is to be deplored, for they provide the only fundamental background for a good doctor, who must have the gift of simple and lucid expression and a wide understanding of people What may be a good background for a scientist is not enough for a good doctor and I therefore condemn these changes wholeheartedly"

Mr Harding mentioned that in the past year Westminster students had derived great clinical advantages from a period of two weeks' resident study at St Stephen's Hospital, he thanked the staffs of St Stephen's and of St Helier Hospital for the enthusiasm they showed in teaching the students.

A change made during the year had been the
of the children's department to Vincent Square
with over 100 beds should be able to provide
pediatrics teaching better than in any other
hospital" The number of students at Westminster
steady at about 220, and applications from
candidates had been considered for 65 places.

Public Health

DRIED BONES AS A SOURCE OF AN

D G DAVIES
M B Brist, Dip Bact.
CLINICAL BACTERIOLOGIST, WELSH NATIONAL
MEDICINE, CARDIFF

R W S HARVEY
B Sc M B Edin, Dip Bact
BACTERIOLOGIST, PUBLIC HEALTH LABORATORY,

MOST cases of anthrax in man in Great
caused by contact with infected hides, wool
but infection has also been acquired from dried
bone products, or horn Crushed raw bones are
used as fertilisers and in various chemical
Bone meal is also used in animal feeding stuffs
for these purposes are imported from many
in some of which anthrax is common among
Large quantities of sun dried bones from the
are imported, and some of these bones are
anthrax spores

In Man—From time to time cases of
be traced to bones or bone products
described 2 cases in the horn industry, a 3rd
hafter, and a 4th in a farm labourer who
meal fertiliser The Chief Inspector of
noted 2 cases in workers in the fertiliser trade
dried crushed bones from India were used
Cheney (1935) described 1 case in a farm lab
developed anthrax apparently from handling
fertiliser in Maine, U S A Jones (1942) reported
human cases in Kent associated with the use
meal, and A J Wilsdon (personal
reported 1 case in a human contact of an animal
from Indian bone meal In 1943 the Ministry of
issued a press notice to agricultural and medical
pointing out that care should be exercised in the
of imported bone meal fertiliser from India
of Health 1950)

In Animals—Infected bone meal has been
as the cause of anthrax in animals as well as
Jones (1942) described 2 cases, and Wilsdon
communication) 5 cases, in cattle, and all were
to be attributable to the use of raw bone meal
Stockman (1911) reported that 83% of cases
farms which had not previously had a case,
thirds of these instances the evidence pointed to
from artificial feeding stuffs or manures Jackson
regarded bone meal fertiliser as one source of infec
farms in Great Britain though he believed
artificial feeding stuffs, such as oil cakes, were
dangerous, but he admitted the difficulty of
relative importance of these two potential
infection In one outbreak described by Jack
cattle, fed in error with bone-meal fertiliser,
anthrax During the 1914–18 war the
anthrax in animals in Prussia and Saxony was
by some workers as correlated with the great
in imports of raw bone meal (Hutyra and Marek

Recently, the increase in anthrax among farm
and the possible association of this with the in
imports of some feeding stuffs and fertilisers
bone meal, have received some attention (Lancet
1953) One of these reports stated that "the

to suppose at present that this has meant any ıe in the incidence among humans. However ᵣo found in one industry 14 cases in six years from ırce

ɪRAX IN FACTORY HANDLING SUN DRIED BONES

-dried crushed bones from India and Pakistan ɜ raw materials in a chemical factory engaged in the ɪacture of fertilisers, glue and gelatin The bones, are crushed to sizes varying from 0 5 cm to 5 cm ported in canvas sacks each holding about 1½ cwt ɜs of anthrax occur among the workers whose ɪt is to stack the bones or otherwise to handle the before the chemical treatment begins. This cal process consists in contact with mineral acids for days, followed by treatment with lime &c long time The resulting fluid is heated and rated under reduced pressure to supply phosphates and gelatin *It is not believed that anthrax or spores would remain viable throughout such* ess.

m 1947 to 1952 inclusive 13 cases of anthrax ed in the workers handling the bones and the sacks. 4th case was in a man who visited the factory to o empty sacks in his lorry a few days later he ped anthrax No cases occurred in any other ɪf the factory and anthrax was confined to those andled the sacks and the sharp crushed dried bones f the 14 cases the diagnosis was confirmed bacterio lly In the other 5 treatment was begun before ıens were taken and it was thought undesirable ɪurb the lesion unduly to get a satisfactory specimen lture

ı laboratory examined thirty samples of bone, three ɪt, four of sacking and two of dried sinews from ıctory Anthrax bacilli were isolated by animal ation from two samples of bone and one of sacking

DISCUSSION

Wales most cases of anthrax in man can be traced ıtact with infected sun-dried crushed bones from ar East As might be expected, the anthrax ıts as a malignant pustule among those workers ɪarry the sacks of sharp crushed bones, and no have appeared in other parts of the factory where ɪnes are chemically treated. In 13 of 14 cases the was on the face or the neck

lff and Heimann (1951) showed that in the United ı of America most cases of malignant pustule could aced to materials imported from the Far East wool was the source of the infection it was not ɪool from Australia but coarse wool from the Far ıused in the manufacture of carpets. When hides the source of the infection they were almost always des from India and Pakistan. Wolff and Heimann tated that in 1947 a million animals died of anthrax ın Anthrax is also very common among animals ı Far East

ndustrial anthrax in Great Britain the origin of the ial seems to be all important Crushed bones are ted into Britain from many countries. The ıts with anthrax mentioned here handled crushed ried bones from India and Pakistan in large ities, and anthrax bacilli were demonstrated in ɪes of these bones *Of the 14 cases reported here* ı was not employed in the factory but was a lorry who removed empty sacks from the factory ɪlar incident was reported by Holgate and Holman)

SUMMARY

cases of malignant pustule occurred in factory ɪrs who handled sun-dried bones from the Far East. ɪther case was in a lorry driver who took away from actory empty sacks which had contained such

We wish to thank Prof J Gough and Dr Scott Thomson for advice and encouragement in the preparation of this paper

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Control of Food-poisoning

Following the recent outbreak of food poisoning in Wakefield,[1] *a recommendation from the city's health* committee is to be placed before the city council[2] It asks that strong representations be made to the Ministry of Health to provide legislation that will enable a medical officer of health to close premises where persons suspected of being carriers are engaged in preparing or handling food The shop involved in the Wakefield outbreak did in fact close voluntarily for two weeks but under existing regulations the medical officer of health's powers are limited to the suspension of employees known to be carriers.

Poliomyelitis

Poliomyelitis notifications (uncorrected) in the week ended Oct 10 (40th week of the year) were (previous week in parentheses): paralytic, 107 (79), non paralytic 69 (78); total 176 (157)

The following table compares this year up to and including the 40th week with the preceding six years:

Year	*Total cases up to and including 40th week*	*Cases in 40th week*
1947	7093	429
1948	1537	66
1949	4023	376
1950	6711	363
1951	2301	96
1952	3483	166
1953	4256	176

There has been an increase of 28 in paralytic cases and a reduction of 9 in the non paralytic cases as compared with the previous week. The weekly notifications at this time of the year are often a little erratic and there is no reason to believe that the reduction in notifications will not be resumed very shortly

Statistics for England and Wales

Provisional figures for England and Wales published[3] by the Registrar-General show that in the quarter ended June 30 1953 the birth rate was the highest for two years. There were 179 404 births registered during the quarter, representing a birth-rate of 16 4 per 1000 population—the highest for any quarter since the second quarter of 1951 There were 114,538 deaths registered in the quarter—a rate of 10 5 per 1000 population which is the lowest rate for a June quarter since 1948 There were 4441 deaths of children under one year of age giving a rate of 25·0 per 1000 related live births. The 4199 stillbirths registered represent 22·0 per 1000 of the total live and stillbirths.

Provisional figures[4] for the third quarter of this year show that the birth rate was higher and the stillbirth and infant mortality rates lower than the rates for the corresponding quarter of 1952 Live births registered numbered 172 976 representing a rate of 15·6 per 1000 population Deaths registered numbered 98,588, giving a rate of 8 9 per 1000 population Deaths of children under one year of age totalled 3832 or 22 2 per 1000 related live births. There were 3709 stillbirths registered—a rate of 21·0 per 1000 total live and still births.

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[1] See *Lancet* Aug 15 1953 p. 339
[2] *Yorkshire Observer* Oct. 3 1953.
[3] The Registrar-General's Quarterly Return for England and Wales: Quarter ended June 30 1953 H.M Stationery Office Pp 47 2s.
[4] The Registrar-General's Weekly Return for England and Wales for the week ended Oct 10 1953 H.M Stationery Office Pp 12 1s

In England Now

A Running Commentary by Peripatetic Correspondents

AFTER a long drive through the parkland and a short approach through formal gardens of juniper and cypress, I was met at the door by Saunders, the butler, who peeled off my coat and took my hat and gloves. I was allowed to keep my stethoscope and book of forms.

I was asked to wait for a few moments, and was glad of the time to inspect the Great Hall with its carved stone fireplace, the oaken screen supporting the minstrels' gallery, the staircase with its wide and gentle tread, and the emblazoned angels peering with irreproachable piety from the hammer beams of the old timbered ceiling. The evening sun streamed in through the great mullioned windows, lancet and oriel, in a thousand fragments of tinctured light, and it was through this misty mosaic of colour that her ladyship descended with a dignity and measure which belonged to more spacious days.

She conducted me along the gallery into a bedroom which, I reflected, must be twice the area of my house and surgery put together. His lordship was enshrined in a four-poster, inhaling menthol and buttressed by a cloud of pillows. From the portraits on the panelled walls, ancestral faces regarded him, some with disfavour, some with dispassion—none with encouragement. Our consultation, including an elaborate clinical examination, took twenty minutes. The diagnosis was flu.

With customary graciousness, her ladyship accompanied me downstairs to the entrance hall. I bade her be of good cheer, for there was little cause for alarm. I felt, and hoped I looked, wise and kind and rather medieval. I was about to drive away, when Saunders hurried down the steps, bearing a silver salver and upon it a paper. "His lordship has just noticed, sir, that you have forgotten to sign his First Certificate."

* * *

What magnificent stuff the Widdicombe File is giving us these days. "ORGS." Absolutely divine. I should think the article will be wonderful too, I haven't actually read that yet. I can't stop thinking about the title. What *can* it mean?

Orgs at last, thought the traveller, gazing from the hill at the tiny town nestling in the marshes below. Orgs, the pearl of Provence as the oyster-hating King René had named it. Orgs, one of the smallest walled cities in the world and the sole to have a wall with the purpose of keeping the inhabitants in. Before these walls, Axel, brother of Charles Martel, had slain 375,000 Saracens[1] with an armoured flit gun without any noticeable benefit. A pall of blue smoke hung over one building in the centre of the town. The Grand Hôtel d'Orgs, smiled the traveller tightening his belt in anticipation of supper. The Grand Hôtel d'Orgs, the solitary hotel in the *Guide Michelin* to have four exclamation marks after it. He strolled down the hill rather nauseated.

Orgs, exclaimed the wickedest man in the world, really what will they do next? Alastair Crowley would have been aghast. It was bad enough when Aldous flippantly referred to orgy-porgies in *Brave New World*, but these people go too far. The ancients would have been shocked. "Is there an org on at the palace tonight, Nero?" or "Splendid org at your place last night, Messina." As for the French masters, they would simply have shuddered. "The Marquis de Sade requests the horror of your company at an org in the château tonight." Really he would go round and see the editor. He would carve it on his chest with an amethyst-tipped lancet (oh, justice), saying through clenched teeth "this will teach you to use abbreviations."

"Orgs, sir," stuttered the keen young houseman, "I think it's Orgs, sir." "This seems to be one of the many conditions newly arisen since I was a registrar," said the surgeon. "Whatever is it?" "Why, sir, Orgs is an occupational disease of cinema organists. The mighty Wurlitzer first described it. It's a state of confusion in the motor cortex, due to the fact that they have to play arpeggios with both hands, pull out the stops, switch on the whistles, bagpipes, and drums, bounce up and down on those wooden both feet, and watch for spelling mistakes slides. Ultimately they do it all the time and, can imagine, they get terrible indigestion." The surgeon threw a sponge holder at the and shouted "Orgs has set in."

I'm looking forward immensely to readin

* * *

John (rising four) and I have got a new machine on which we do our sums. We have owned one, but never a machine that electricity nor one with so many buttons. It of 1's, 2's, 3's, &c, for adding or taking away, row of buttons that show an impetuous start multiplication. It will give us an answer figures though we don't usually want all rate it almost as high as a cash register. (" you have today, Sir? Rice is nice and Concealed in it are unsuspected depths of count tion. Clear the registers and take away 1 from What's the answer? At school it may be minus on our machine it is quite plainly 9999999999. This result reduces John to helpless laughter cannot press another button for at least ten. It is not, however, his favourite sum, which centres round the number 6, admittedly a good number, usually honest and dependable. He multiply 6666666666 by 6666666666. Curiously the result is 44444444435555555556 which has attractive symmetry. My own favourite is to 355 by 113. The machine works the answer itself, and returns to the starting-point in haste. There is just time to gulp a cup of it is not too hot. The result is 3 141592920, to 6 places of decimals; we have tried a lot fractions but they are all quite hopeless. T us that π is not only irrational but tran- we haven't got as far as that yet. Alt wonderful machine and it lacks only one bell that rings when we do the sum right.

* * *

I approbate that mother who wrote to the mistress protesting against Maggie being taught logy. "It don't do her no good, and only rude." I hold that to attempt to educate the by health talks is to do them disservice. It all very well. Teach people to be clean, to their teeth, to eat, drink, and smoke in and to take regular open-air exercise. But to tell to look for the early signs and symptoms of disease? I think not.

We ourselves are bad enough in our of subjective occurrences. Which of us has recognise in himself heart-disease or malignant I have always supposed myself to be relatively this foible. But last week revealed that I am no than my betters.

Weakness of my right hand and various sensations in the upper limb set me on the differential diagnosis. Was I conscious of some tory difference, could I detect dissociated or wasting of the thenar muscles? Attempts at investigation are conspicuously clumsy and attracted attention. "What on earth are you asked she who insists on knowing everything facedly I described my symptoms and the fears had occasioned. "Don't you think that bed-making for the first time at your age might something to do with it?" said she, who if she respect for such academic distinctions as M.D. successfully conceals it.

* * *

Overheard at an interview for a post of county of health in Ireland.

Member of Selection Board. "The League of Nations collect international epidemiological information, looks after it now?"

Candidate. "I don't know."

M.S.B. "But I've just told you."

Candidate. "Who?"

M.S.B. "That's right."

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[1] Ancient Provençal word for mosquito.

Letters to the Editor

STRIC RESECTION FOR HÆMORRHAGE

—In the search at operation for the cause of æmesis and melæna Mr Ferguson (Oct 10) like the limit drawn at laparotomy followed use of eye and hand on the outside of the viscera abnormality is found he advises a burst of activity form of passing through the motions of one's ite brand of partial gastrectomy in the hope sume that this shot-in-the-dark technique will he lesion in the bag I agree he will probably be or 8 or 9 patients out of 10 But what of the other ? *They may well bleed on* and one has seen it n, that a pretty partial gastrectomy was performed e bleeding ulcer was left behind

s by no means rare to find no external sign of an at laparotomy for gastroduodenal hæmorrhage *ect at gastrotomy one or more acute ulcers, from* ghth of an inch to one inch or larger in diameter be found These ulcers, in my experience are singly common in elderly women and are usually posterior wall in the middle third but sometimes may be found high on the lesser curve or may be in the fundus on the posterior wall Worse the bleeding points may be deeply down the num more than two inches from the pylorus e seen two such ulcers one being partnered by an gastric ulcer which at first was *thought to be the* of hæmorrhage the bleeding duodenal ulcer being overlooked and left in situ

strotomy, even duodenotomy if necessary are the ways of finding the exact site of trouble and so ing that the operation is not followed by continued ng Mr Ferguson does not care for gastrotomy it is not justified by the soiling and loss of blood alls and that the view inside is a poor one owing adherent blood-clot Perhaps we do gastrotomy fferent ways, for I find it helpful in locating the

stomach is lifted into the wound and towels placed it to prevent soiling An incision about four to six long is made along the middle of the anterior surface stomach *starting at the antrum* and usually stopping before the point is reached where the customary transsection is made The cut edges are grasped by Duval which reduce bleeding to a trifling trickle Large clots are cleared out by hand and large retractors of the or Deavers variety (not the sharp-edged Morris retractor cuts the mucosa) suction, and wet or dry swabs are a good light is focused into the lumen and the whole r of the stomach can be seen as clearly as if looking *ht into the inside of a barrel* A *finger is passed* into uodenum and if necessary both the remnant of the m and the pylorus may be cut through, and even the or wall of the duodenum may be incised for about one The view is magnificent, and is unobscured by blood If no source of bleeding is found the edges may be and safely sutured with no serious reduction of lumen. ilst the stomach and duodenum are open and no satis cause has been found it is still possible to make a search of the lumen using a sigmoidoscope to get down the duodenum Also jejunotomy can be done itroducing the sigmoidoscope The jejunum is folded the sigmoidoscope in concertina fashion an excellent of the mucosa being obtained A long bronchial sucker reat help in clearing the way

no ulcer is found after such methods and an œso eal source of bleeding has been excluded it is fair to do partial gastrectomy on an empirical I have *a personal preference* in these patients dding a vagotomy to partial gastrectomy perhaps more empirically

gree with Mr Ferguson that it is not safe to close bdomen without making an attempt to stop the ing but I prefer to avoid blind partial gastrectomy and to stick to the fundamental principle of surgery—adequate exposure of the lesion

Radcliffe Infirmary
Oxford.

G E MOLONEY

SIR,—Mr Ferguson draws attention to a very real problem of surgical management I agree that with the exclusion of external evidence of a gastric or intestinal lesion it is right to proceed with partial gastrectomy for bleeding without wasting time doing a gastrotomy I would like to add two points Firstly the surgeon should split open the stomach immediately it is removed and inspect it within Secondly if he finds no obvious erosive gastritis ulcer or other cause of hæmorrhage he must inspect the inside of the *remaining* gastric fundus

I have seen two patients in whom a very high peptic ulcer was missed by external palpation; and in both instances hæmorrhage persisted after partial gastrectomy and proved fatal In one case I was the assistant and was astonished to see at autopsy quite a large chronic ulcer high up on the splenic aspect In the second case I operated myself and the same thing happened At autopsy a shallow ulcer about 1 in in diameter was found close to the œsophageal junction on the posterior wall of the stomach The crater was traversed by a large artery which had bled from a longitudinal clean-cut slit. Even at autopsy when the gastric remnant was removed, this ulcer could not be felt externally I believe that, in each case the patient's life could have been saved if the gastric fundus had been inspected directly and the offending vessel dealt with from inside

From my own experience of the type of case discussed by Mr Ferguson, where a laparotomy has been considered necessary for severe bleeding I would strongly advocate *partial gastrectomy at any age*

Liverpool

JOHN A SHEPHERD

PAIN IN CHRONIC GASTIC ULCER

SIR,—Discussions on the relation of gastric ulcer to pain are hampered by the lack of a common viewpoint in psychology and medicine. Pain is always associated with pattern-changes in the vascular flow in the tissues and the cardiovascular system is as much an organ of pain as the brain is the organ of the mind Psychiatrical conditions can be discussed in terms of vascular flow[1] and incomprehensible titles such as The Internalized Mother as Harmful Food in Peptic Ulcer Patients[2] would invite study if the meanings the authors intended to convey were related to particular tissue ischæmias and hyperæmias and associated with frustrations and compulsions respectively

Acid kills cells, and amongst other changes, damaged cells become acid and acidify neighbouring cells—the primary origin of pain The central nervous system ensures instant sharing of the acidity by distant cells of the body (nerve impulses being equivalent to a transfer of hydrogen ions or acidity) thus saving the damaged cells from destruction where possible The part played by the vascular system is mainly a removal of acid metabolic products ischæmia increasing the acidity in any functioning tissue

Specific reflex pathways are mechanised by modifications of the cerebral synaptic resistances, which can be expressed in terms of local blood flow in the neuropil[1] The sensitisation of nerve-endings by tissue degeneration products *may be considered as a decrease of tissue* (synaptic) resistance with hyperæmia and congestion The protection of nerve-endings by mucus is an ischæmic insulation of the nerve-endings Tissue tension distorts the vascular network giving patchy ischæmia and hyper emia (cancrum oris without oedema is painless) Tissue acidity is a cause of dilation of blood vessels The cerebral patchy anæmia in melancholia is relieved in some cases by the vasodilating effects of electroconvulsive therapy, and the congestion of the motor cortex in general paralysis makes the patient happy—the two clinical conditions representing chronic pain and its opposite, respectively

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[1] Pickworth F A New Outlook on Mental Diseases Bristol 195[illegible]
[2] Garma A *Int J Psycho-anal* 1953 34 102

There is therefore no need to choose between the "acid"[3] and the "inflammatory" hypotheses, since both are ultimately true, but expressed in different terms As Mr Kinsella shows in his reply[3] to Professor Pickering (Sept 19), to state the problem in terms of vascular flow does clarify in a general way the meaning of his article[4]

Birmingham F A PICKWORTH

"CHEMOTHERAPEUTIC AGENT" AND "ANTIBIOTIC"

SIR,—I read with interest Dr Glass's letter last week I found it desirable to suggest (Aug 29) a more exact literal definition of "chemotherapeutic agent" than that offered by Professor Waksman, but had not intended to imply that the literal interpretation is in use or should be used "Antibiotic" in its etymological sense refers to something "against life," and, as someone else has already asked, "Whose βιοσ is it?" To follow this line of thought, *aspirin could be described as an antibiotic*, for, if ingested in sufficient quantity, it destroys the life of man, but none would insist on such literal accuracy

Although the terms "antibiotic" and "chemotherapeutic agent" both have much more limited meaning than their etymology would suggest, it does appear from the correspondence that agreement has not yet been reached as to what exactly they should mean After all, this is what one should expect of terms recently coined, and, therefore, still evolving

Frodsham, Cheshire G S ERWIN

RESETTLEMENT OF DISABLED PERSONS

SIR,—Your annotation (Oct 10) is not only unfair but it demonstrates clearly the self sufficiency of some doctors which has in fact been one of the greatest difficulties in resettling the disabled The purpose of your annotation seems to have been a denial of any good that the Ministry of Labour and National Service might have done in recent years, and a belated recognition of the achievements of a few medical pioneers in the past You remind us of the report of the British Medical Association Committee on Fractures in *1935*, the Government inter departmental committee in 1939, the rehabilitation of miners in 1940, and a few other such activities In so far as I myself was partly or largely responsible for many of them I can the more readily ask what this has got to do with the endeavours of today Let us be rid of this complacency

The Ministry of Labour has tried hard to implement the proposals of these pioneers, and in so doing has never lost an opportunity of collaborating with the medical profession Of course there have been failures—who would have expected otherwise in a scheme of such magnitude? It is because this great social service (and whatever you may say it is still ahead of any similar service in any other country in the world) has shown defects in its first few years of trial that the medical committee and the National Advisory Council have persuaded the three Ministers concerned to re examine the position

But for you to write that "perhaps the findings of the present committee of inquiry may point the need for fuller recognition of the medical implications of disability" is *little less than arrogance* This has been the endeavour from the beginning, and if in this respect there has been failure it lies more with th profession than it does with the administration,

As a simple illustration of this, let me quote annotation, which refers to doctors who are because "they have been discouraged by its give effective help to those patients whom referred to it" Did these doctors really think duty was done when they had signed a form of Did they believe that nothing more was expected than to sign a name? In the interests of their the aid of the disablement rehabilitation office, the improvement of the service, why did they more about it?

I will not bother your readers with the success that has been achieved in nearly one disabled persons in Great Britain Neither will the mistakes of which we are all aware But I that every physician, surgeon, and general p should find out for himself how great a service being offered for disabled patients and ask only doctor should use the service intelligently, and improve it by thoughtful collaboration rather thoughtless criticism

REGINALD WATSON-JO
Chairman Medical Advisory C
National Advisory Council f
Resettlement of the Disabl

London, W 1

BARBITURATES AND ALCOHOL

SIR,—Apropos the recent discussion on this in the lay press and in your columns,[1] here is of Boris

Boris is a colossus of a Slav He carries his fif becomes a professional soldier, though he is now worker in mosaic But, like Achilles, he has one —his stomach Ever since he "did duty" in the salt mines he has been a martyr to indigestion.

When I first met him on admission he was deeply c His normal ruddy complexion had become that of a Victoria plum *His breathing was stertorous*, and showed signs of early aspiration pneumonia His was 101°F He was thought to have attempted s 'Nembutal'

Following gastric lavage, twelve hours in an oxy and suitable doses of penicillin, he regained con and proved to be more sinned against than sinning

Apparently on the evening before admission he h severe bout of indigestion Friends had persuaded h panacea for all ills, including indigestion, was lar strong beer Accordingly he drank ten bottles of 'Sp

On arriving home he still felt uncomfortable, so h three *capsules of nembutal* which had been prescribe doctor for sleeplessness He went to bed, and sank oblivion that lasted twenty four hours. A dem barbituric acid was detected in both blood and urin

The General Hospital,
Birmingham
J D C

HYPERPOTASSÆMIC PARALYSIS

SIR,—I am very much indebted to the ar Professor Bull and his associates in your issue of They have, I think, given me the answer to the death in two very interesting cases which I saw and which I have reported elsewhere[2], for until their article I was in ignorance of the earlier work they cite

Briefly, the history in each case was similar patients had renal suppression of relatively slow and before the suppression had continued long to give cause for immediate alarm, they deve rapidly ascending flaccid paralysis involving first muscles of respiration and resulting in death wit hour of its onset The mental condition of h perfectly clear to the end

At the time I was very puzzled about the I had no facilities for estimating the serum elect and knowing that because of the renal failure th

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[3] Kinsella V J *Lancet* Oct. 10 1953, p 780
[4] Kinsella V J *Ibid*, Aug 22 1953 p 353

[1] See annotations *Lancet*, 1953 i, 1140, *Ibid*, Sept 19, 19
[2] *Med J Aust* 1951, ii, 9

im level was very probably high I did not
r this level to be a likely cause of the condition
careful investigation of post mortem material
ed that thrombotic thrombocytopenia was the
f this rather unusual form of decease I am now
r much more certain that these two deaths were
o to hyperpotassæmia

x Victoria,
stralia.

David C Wallace

PERIODIC MEDICAL OVERHAUL

-Dr Capel (Oct 10) ascribes to me surprise that
prehensive clinical examination failed to reveal
nt disease, and then, somewhat gratuitously
s to remind me that there is a stage in every
before which diagnosis is impossible and that
ill are many diseases which, however early they
eted are incurable
ently he has failed to appreciate that I described
xperiences as the text of my thesis in disparage
the claim advanced in favour of periodic overhauls
rly evidence of trouble may be discovered and
l. To illustrate the value of the periodic overhaul,
ances the investigation of such symptoms as
indigestion piles, bronchitis menorrhagia flat
d varicose veins—symptoms for which any sensible
would seek advice I must again point out that
ponents advise the overhaul *when well* (I repeat
les employed in my original contribution)
Capel concludes by advocating a course of instruc
help the individual to adjust himself to his
ment; to avoid over eating over drinking and
unhygienic habits and a bad mental approach
g domestic discord to learn about suitable
y and the evils resulting from lack of hobbies
sumably an indefinite number of similar matters
a very different thing from a medical overhaul
nmon sense health education which should receive
earted approbation although I am by no means
led that a doctor is the best choice for such
tion

n W 1

Adolphe Abrahams

NE MEMBRANE IN THE NEONATAL LUNG

-We are grateful to Dr Claireaux (Oct 10)
onstrating the importance of hyaline membrane'
use of death in infants in this country but his
t of the theory that the membrane is produced
linised epithelial squames is I think unfortunate.
fants dying a few weeks after birth keratinised
keratinised squames are frequently found and
ccompanied by any reaction or hyaline membrane
squames can also be seen embedded in, but
from the hyaline deposits in hyaline membrane
in the newborn
results of Dr Claireaux's experiment with auto
mniotic debris are not necessarily related to the
disease indeed it would be surprising if any
ous hyaline material injected into the lung of
l not show a deposit or membrane production
of six animals thus injected
line membrane is found in the lungs in children
the newborn period dying from nephritis
tic heart-disease and some deformities of the
These membranes are virtually indistinguish
om those seen in the newborn and any theory
production of hyaline membrane in the newborn
, I think take these other similar membranes'
onsideration In the older group it is unlikely
he deposits are in any way related to inhaled
al and the most obvious common basis is some
nisation of vascular circulation within the lung
ewborn child sustains great physiological changes
monary circulation during the transference from
tal to alveolar oxygenation and it would seem likely that it is in these intrapulmonary vascular changes associated with birth that the prime factors leading to hyaline membrane production arise

Department of Pathology
The Children's Hospital Sheffield.

John L Emery

THE WRONG BLOOD

Sir,—You may delegate administrative responsibility but if you divide it you invite chaos The pathologist must administer the blood bank hence he should supervise the chain of demand and supply between patient and blood bank even though the clinician may order and inject the blood The argument is reinforced when the clinicians are mostly part time and the pathologist full time

Study your problems with diligence,' ' look not for refuge to anyone beside yourself ' are maxims for a consultant and if the pathologist follows them, his advice and help will be valued Let him wriggle out of responsibility which is naturally his, and he will forfeit the respect of his colleagues In this country it has always been assumed—in contrast to the suggestion made in Dr Walther's letter last week—that clinical pathologists are concerned with clinical matters, not with techniques alone

Central Middlesex Hospital
London N W 10

George Discombe.

ACUTE ANURIA

Sir —In discussing the treatment of anuria your leading article of Aug 22 lays emphasis on the need to correct the water and electrolyte disturbance Thus your approach is essentially symptomatic, for these changes are *secondary* to the renal dysfunction It is to be regretted that the primary change in the kidney is so lightly touched upon

The reader is left with an impression that a depleted blood *volume* leads to anæmia of the kidney—though ischæmia has been its designation—and that this is responsible for the anuric state. This interpretation ascribes to the kidney a *passive* rôle which is readily denied by its failure to recover when the blood volume has been restored and still more emphatically by an assessment of the various factors that precipitate anuria *Among these Darmady*[1] *includes acute pancreatitis* emotional states head injury myelomatosis typhus fever Weil's disease pneumonia favism mushroom poisoning streptomycin burns, crush injury septic abortion and many other conditions not associated with a depleted volume of circulating blood In acute glomerulonephritis, which you cite as an occasional antecedent not only is there no reduction in blood volume, but renal ischæmia is also not evident. For Bradley[2] has shown in this disease that if the extraction rate of *p* aminohippuric acid (P A H) is concurrently determined the renal blood flow is found to be increased. Yet the increase in renal blood flow is associated with reduced glomerular filtration. Such an alteration in renal hæmodynamics cannot be explained by a passive change in the kidney for it proclaims an unequal distribution of vasomotor tone within the organ determining the blood flow through its components.

It may be that you are inclined to attach lessened significance to biochemical interpretations in this connection because the popular concept of urine production with which such data are correlated has been weakened by the researches of Platt,[3] Borst[4] Wirz[5] Brodsky and Rapoport,[6] and many others. Or because confidence in it has been shaken still further by the experiments of Harvey L. White[7] who on explanting the bladder base and sampling the ureteric outflow, found that partial compression of the renal artery of one side reduced the water and sodium output by 50% on that side without any detectable change in glomerular filtration rate or in tubular extraction Nevertheless you say that "cogent evidence has been brought against the idea that blood is diverted from cortex to medulla and juxta medullary glomeruli"—which means that you are prepared to attach greater importance to inferential biochemical data than to actual visual proof [8–13]

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[1] Darmady, E M *Proc R Soc Med* 1952, 45 811
[2]. Bradley S E., et al *Amer J Med* 1950, 9 65
[3] Platt R. *Brit med J* 1952, i, 1313 1372.
[4] Borst J Personal communication 1952
[5] Wirz, H., Hargitay B., Kuhn W *Helv physiol acta* 1951 9 196
[6]. Brodsky, W A., Rapoport S *J clin. Invest* 1951, 30 [illegible]
[7] White H L. *In* Bradley S F., Renal Function New York 1950; p 128

Lovgren's [14] experiments on the frightened cat have shown that adrenaline stimulation does provoke the Oxford mechanism, and they offered an explanation of the "afferent" and "efferent" glomerular spasm which has been held responsible for the alteration in renal hæmodynamics which adrenaline produces From this it would be reasonable to assume that diversion of renal blood flow comprises a series of stages dependent on progressive alteration of intravascular tone (Sophian [15 16]) and based on the underlying principle of critical closing and critical opening pressures (Burton [17]) The experiments of Van Slyke et al.[18] do not deny its occurrence, but rather suggest that the Trueta reflex mechanism may not be provoked if the stimulation is too gradual, even though it continues and destroys the subject On the other hand, the evidence derived from the experiments of Insull et al [19] cited by you are hardly acceptable, made as they were on well nigh moribund animals in which all trace of the vascular tone responsible for the reflex had long since disappeared The theory of maximal tubular clearances on which much of the "cogent" evidence has been founded, although brilliantly conceived, can hardly be considered final We are left to conclude that the visual evidence supporting the Trueta mechanism must far outweigh the inferred evidence, and that cortical ischæmia is accompanied by diversion of blood to the medulla

The catadromous fish (e g, salmon and eel) also offer evidence of renal shut-down on change of environment (Homer Smith [20 21]), this effect being seen when they move from fresh water to the sea Further, it has been shown experimentally that renal ischæmia of the Oxford pattern precedes acute cortical necrosis Franklin and Sophian,[22] demonstrated this by stimulating the renal nerve Also Hoff [12] has shown that long-continued electrical excitation of the cat's brain produces cortical ischæmia and medullary congestion in the kidney, leading to acute tubular necrosis

In citing Oliver [23] you have perhaps lost sight of the fact that many of his nephron dissections were performed on Shaw Dunn's original specimens Shaw Dunn and Montgomery [24] established that these anuric kidneys with cortical destruction displayed subcapsular, juxtamedullary, and medullary survival, but you say nothing of this evidence which supports the then unheard of Oxford mechanism, although you admit that ischæmia is responsible for the cortical damage Further histological evidence has been provided in particular by Solymoss,[25] De and Sengupta,[26] Borst,[27] and and extensively by Sheehan [28] in a review of post mortem material Sheehan has shown complete cortical necrosis the spasm affects the end of the arterial tree at a distance of 0·5-1 from the origin of the intralobular artery, which the survival of the juxtamedullary nephron indicates a vasomotor alteration and therefore a rôle for the kidney

Biopsy of the anuric organ, by punch or by exp supports the view that cortical ischæmia and m congestion are concomitant

The experiments (of Franklin and Sophian demonstrated the mediation of the nervous changes of intrarenal vascular tone (Hoff [1]) ability of the kidney to recover if the changes very advanced Evidence is also forthcoming rapid establishment of diuresis by certain t methods, that the tubular state is reversible e late on This has been demonstrated by Dérot peritoneal dialysis, by Vallery Radot [30] with transfusions, by Hingson [31] with conduction an reaching the lesser splanchnic level, by Chat with vitamin C and anti histamines, and by O and Spitzer [33] with paravertebral block In inte the effects of intraperitoneal dialysis and of transfusion, a rapid correction of the milieu is implied which is comparable to the physiological over of the catadromous fish in re-establishing function when resuming a fresh water habitat

The association of blocked tubules with fatal merits consideration The obstructing material to be a myohæmoglobin derivative But globin itself has been shown by Franklin [34] to diuresis In a normally functioning kidney th stance cannot be held responsible for the renal In fact, Yuile et al [35] found that a short period ischæmia was necessary for hæmoglobin casts produced in the rabbit, whilst Badenoch and Dar have shown that, in rabbits, mechanical reduction renal circulation for 90 minutes, together with of stroma free hæmoglobin, causes a higher than either procedure alone It therefore seem tubal blockage of this type implies a preceding ischæmia (In cases of incompatible transfu early accompanying anoxæmia could have the renal shut down, whilst in crush injury th experiments have underlined the ætiological st Accepting that a gradual failure of glomerular f accompanies the diversions of renal blood flow that the filtered substances (innocuous in will tend to accumulate in the tubules and form ing and insuperable barrier to urine secretion cortical ischæmia has been overcome In the stages of the failure denervating the kidney by con anæsthesia could prevent this, and the accum material would then be continuously voided if an underlying and associated anoxæmia ha responsible—as in cases of incompatible trans measures directed towards reducing this an reduce mortality

We should recognise, I believe, that the " ischæmia " persists in anuria but can be overcome

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8 Trueta, J, Barclay, A E, Franklin K J Daniel P M Prichard, M M L *Studies of the Renal Circulation* Oxford 1947
9 Franklin, K J *Proc R Soc Med* 1950 43 467
10 Franklin K. J *Ibid*, 1949 42, 721
11 Daniel P M Peabody, C N Prichard M M L *Quart J exp physiol* 1952 36, 199, *Ibid*, 37, 11
12 Hoff E C et al *J Neurophysiol* 1951 14, 317
13 Kramer K et al *Int physiol Congr* 1950 p 314
14 Cited by Franklin K J, Ciba Symposium on Circulation 1951
15 Sophian G J Ciba Symposium on Circulation, 1951
16 Sophian G J Toxæmias of Pregnancy (in the press)
17 Burton A C *Int physiol Congr* 1950 p 139
18 Van Slyke D et al *Amer J Physiol* 1946 145 314
19 Insull W jun Tillotson I G, Hayman J M jun *Ibid*, 1950 163, 676
20 Smith H W *Ibid* 1931 98, 279
21 Smith, H W *Ibid* p 290
22 Franklin K. J Sophian G J *Proc R Soc. Med.* 1951, 44, 399 401
Oliver J MacDowell, M Tracy, A *J clin Invest* 1951, 30, 1307
nn J S, Montgomery, G L *J Path Bact* 1941, 52, 1

25 Solymoss, A *Lancet* 1949 i, 957
26 De S N Sengupta, K P *Ibid*, 1951 ii, 1100.
27 Borst J J G Personal communication, 1952
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29 Dérot, M. *Journées méd toulousaines* 1951
30 Vallery-Radot P Cited by Dérot, 1951
31 Hingson R A Lecture at the Royal College of Ob and Gynæcologists, 1948
32 Chatterjee H N *Lancet*, 1952, ii 90
33 O Sullivan, J V, Spitzer, W *J Obstet Gynæc* Br 1946, 53 158
34 Franklin K J Cinefilm demonstration at the Roy of Medicine 1950
35 Yuile, C L, Gold, M A Hinds E G *J exp Med* 1945
36 Badenoch A W Darmady, E M *Brit J exp* 29, 215

ery latest stages. Instead of dealing with its
d allowing it to continue we should deal with
y

unately for the acceptance of the Trusts
of renal blood flow the renal syndromes it
tes can be countered with some degree of
y attacks on its flanks But the frontal assault
ve us both better results in practice and a
derstanding of renal problems

JOHN SOPHIAN

ERATION OF SENIOR PRACTITIONERS

ome six months ago you kindly published a
which I pointed out that I and others in a
sition, were likely to lose £100 a year owing
anckwerts award I was somewhat severely
r this letter but it has alas turned out to be
ified. The £100 has now vanished into the
others

s. GORDON WARD

THE DRUG BILL

t is often possible to add some suggestive to
erapy by prescribing an elegant and useful
y preparation as a change from the sometimes
tive *National Formulary* equivalent The
name or interesting method of presentation
onfidence to the manner in which it is prescribed

y be an abuse of the placebo but it is very useful
e

GENERAL PLACEBITIONER

UDET ARTHROPLASTY OF HIP

he formation of a bursa around the stem of
rosthesis which protrudes through the lateral
rtex does not appear to be generally recognised
of pain following arthroplasty This complica
red in the two following cases

-A woman, aged 60 nine months after operation
of pain in the region of the greater trochanter on
Examination showed a swelling beneath which the
crylic stem could be felt. At operation the bursa
ound to lie beneath the iliotibial tract was excised
truding stem resected

-A man aged 58 twenty two months after bilateral
y noticed aching on the lateral aspect of the left
nation revealed a small tense bursa in which the
tem could easily be palpated The position of the
f the prosthesis, in serial radiographs, showed that
f absorption of the femoral neck beneath the head
thesis the stem had shifted laterally about $^3/_4$ in
nd the protruding stem were resected.

tients the pain was relieved
ients since have had resection of the tip of
ling stem for pain in the region of the greater
but in neither case was bursa formation
clinical examination.

nt of Orthopædics,
pital, London S E 1

N T HOLDEN

LEGAL RESPONSIBILITY IN BLOOD-TRANSFUSION

James (Oct. 3) must surely have misunder
whole object of my letter (Sept. 26) and he
considerations which cannot be discussed
in correspondence columns

me I feel it is essential to point out that many
d disagree categorically with his statement
llergic manifestations of migraine are quite
se of other allergic conditions—asthma,
and nettlerash—in that migraine cannot
on allergic grounds and that skin tests are
ive. The histamine skin test is positive in a large percentage of cases of migraine and a number of us consider that it is treatable by desensitisation with neostigmine [1,2] as well as by other methods

This goes to support my contention that if asthma, hay fever and nettlerash are contra-indications to being a blood-donor then migraine should also be included. Whether the three former really are capable of being transmitted in the weak dilution which is probable in the pooled fluid is a matter about which Dr James knows far more than I do

London W 1

NEVIL LEYTON

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1 *Lancet* 1953 i, 444

GRADING OF S H M O s

SIR,—The statement concerning the review of senior hospital medical officers which you published last week (p 829) calls for one or two comments

(1) "The Ministry replied that the status of all the practitioners originally graded as S.H.M.O had been thoroughly reviewed on more than one occasion

This is categorically untrue. I cannot say how many are in my position but probably I am not unique in that my case has been reviewed once only Such cases must be well known to the Ministry's officials. Of course a review may have taken place without the victim having been appraised of it Perhaps this is what the Ministry means.

(2) The original grading of S.H.M O was made as a provisional status to cover those practitioners who were more than registrars but did not quite measure up to full consultant status. In 1949 it was clearly held out that good work would lead to promotion, and the grading of S H.M O would gradually cease. If subsequently it has been found convenient" not only to retain the grading S.H.M.O but to increase the numbers of practitioners so graded in such a way that soon S H M O.s will outnumber consultants in some specialties, then such a convenience should not be adopted at the expense of practitioners graded before the change in policy Surely these are entitled to a no-detriment clause As matters stand at present the Ministry can be fairly charged with a breach of faith

(3) What is probably more important than this injustice to individuals by the Ministry is the effect of the Ministry's statement on the development of the health service This statement will have the effect of fixing a "caste system—where the Ministry has been pleased to call you there you stay for life No allowance is made for original and useful work. It is no argument to say that the individual can change his job; the Ministry's officials know probably better than most that such advice is merely adding insult to injury for they themselves take care that, in some specialties at any rate an insufficient number of consultant posts is advertised. If it is now difficult to fill house posts because of the past and present policy regarding registrar status I submit that further freezing into a caste system will choke off most newcomers to the profession whose mistaken idea it is that they might contribute usefully to medicine by actually working A caste system which refuses to admit for consideration original work must inevitably mean that the most important thing in medicine is to get to know the right people on the right committees. As this can only be done in "centres" the least the Ministry's officials should do is to stop saying that the health service is improving conditions and standards at the periphery The reverse is now in process and what little good the health service has done to improve peripheral medicine will now be undone Is this the intention?

There is no real difficulty in the situation if the Ministry does in fact not wish to destroy an important part of the health service fabric All that is required is that without changing the establishment of a given post, an individual may on proving his worth be upgraded himself the post to revert should he leave it. If this minor modification is unacceptable to the Ministry as a principle of simple justice then the charge of bad faith, not only with S H.M O.s but with the whole profession of medicine, will be substantiated

S.H M O

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1 Pelner L., Aibel, M E *J Lab clin. Med.* 1942, 27, 1546
2 Leyton N Migraine and Periodic Headache A Modern Approach to Successful Treatment. London, 1952.

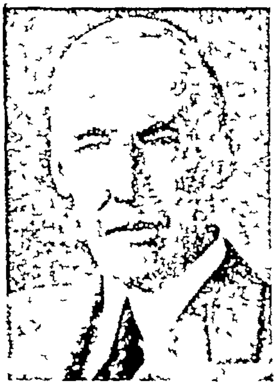
Obituary

EWEN JOHN MACLEAN

Kt., T D, M.D, LL D Edin, D.Sc Manc., LL D Wales, F.R.C.P, F.R.C.O.G, F.A.C.S, F.R.S.E, D.L

Sir Ewen Maclean, who died in Cardiff on Oct 13 at the age of 88, was the doyen of the profession in South Wales and of his specialty in the country generally Born of Highland parents, he was brought up in Carmarthen and attended the local grammar school, from which he proceeded to Edinburgh University He graduated as M.B with honours in 1889 and as M D, also with honours, in 1891 He later became M R C P and he was elected F R C P in 1922

After holding a resident appointment in the Bristol Women's and Children's Hospital, he went to the Chelsea Hospital for Women as a registrar and there started his life's work in obstetrics and gynæcology In 1901 he was appointed the first honorary gynæcologist to Cardiff Infirmary (later Cardiff Royal Infirmary) and he served with distinction in that office until he retired in 1931 with the rank of consulting obstetrician and gynæcologist On the creation of the Welsh National School of Medicine in the University of Wales in 1921, he was appointed professor of obstetrics and gynæcology, a post which he occupied for ten years From the time when he went to Cardiff he had been the pioneer of obstetrics and gynæcology in South Wales He built up a large private and hospital practice and impressed both academic and local authorities with the importance of this subject, especially in relation to maternal mortality and to maternity and child welfare


[Western Mail and Echo

As a clinician Sir Ewen was conscientious, thorough, and conservative, while his teaching was clear and to the point His ability to recall incidents in his vast clinical experience and to deduce general principles from these added to the weight of his instruction, while his long-headed sagacity in surveying the various aspects of a difficult case was illuminating It was, however, as an administrator and in council that his greatest gifts appeared, and this led to his being a member of innumerable committees and chairman or president of many of them He was for years a member of the council of the British Medical Association and was chairman of the representative body from 1910 to 1912—during the stormy days when Lloyd George's National Health Insurance Act was being hotly debated In 1928 when the annual meeting of the B M A. was held in Cardiff, he was elected president and later he became a vice-president His local work for the association included the presidency of the South Wales and Monmouthshire Branch, and the chairmanship of the Cardiff Division and of the contract practice subcommittee of the Welsh Committee He was one of the founders of the Royal College of Obstetricians and Gynæcologists, of which he was a foundation fellow For many years he served on the college council, and in 1935 he was elected president, an office which he occupied with his usual ability and distinction until 1938 In the early formative years of the college his wise counsel and far-seeing wisdom were of great value in the guidance of affairs, and he was largely responsible for laying the firm foundations from which the college has grown to its present position The honorary fellowship of the college was conferred on him in 1947 when the college received its Royal Charter When the National Health Service was introduced in 1948 he was appointed one of the original members of the board of governors of the United Cardiff Hospitals and he served in this capacity until shortly before his death

In the first world war Maclean was adjutant to the Third Western General Hospital in Cardiff with the rank of Major R A M C (T F), and in 1917–18 he the Eaton Hall Officers' Hospital, at Chester, rank of lieutenant-colonel, and later the Third General Hospital

Many honours were conferred upon him He wa of the peace for the City of Cardiff and a deputy of the County of Glamorgan In 1927 the American Surgeons gave him its honorary fellowship, whi he received the honorary degree of M D from the of Melbourne in the course of a world tour which on behalf of the British Medical Association. He the honorary doctorate of laws from Edinburgh U in 1933 and from the University of Wales in 19 University of Manchester made him an honorary 1940 He was knighted in 1923

“ Sir Ewen Maclean,” writes a friend, “wa the old school, but he was one of the best that school He witnessed the growth and dev of modern obstetrics and gynæcology and wa alive to the significance of each advance in Personally he was one of the most charming —kindly, urbane, and patient. His ethics and of social conduct were rigid and he looked for qualities in those with whom he worked A kn *delightful colleague, it was a pleasure to* work and those of us who will not again see his tal guished figure will for long mourn a staunch an outstanding public personality ”

Sir Ewen, who was a bachelor, was the brother of Sir Donald Maclean, at one time of the Board of Education

I WALKER HALL

M D Manc

Dr Walker Hall, emeritus professor of path the University of Bristol, died at his home at on Oct 9, at the age of 80

He qualified at Manchester in 1890 and three later took his M D In 1906 he left Manchester, he was lecturer in pathology, to go to Bristol as gist and bacteriologist to the Royal Infirmary, 1909 he became the first professor of pathology university He relinquished the chair in 1933 to the first director of the department of pre medicine at Bristol, and until his retirement in worked, in conjunction with Prof R H Parry, up the new department which included the la of public health, the public analyst, and pathology

Dr Walker Hall's work in the interests of health became known throughout the world D early part of the century he worked in close collab with Dr D. S Davies on the problem of the carrier , and, following in the footsteps of William he aided the medical profession in the problem of fever In 1916 he made valuable laboratory investi in connection with cases of bubonic plague in over four hundred rats were examined, and the flea, which is the common transmitter of the bacillus, was found His interest in the bacter control of pasteurised milk is shown by the his articles on the subject

He retired seventeen years ago, and began to for the Bar, but his studies had unfortunately discontinued owing to the illness of his wife.

R H P writes “ He was a most loyal chief, those who knew him in the early days of the pre medicine department thought very highly both personal attainments and of his administrative He was a great lecturer and teacher and a most ch companion ”

WILFRED JOHN PURDY

M.B Edin.

Dr Purdy, who died on Aug 28, was best kno his work on filterable fowl tumours, largely ca in collaboration with the late W E Gye He in 1882, in Derbyshire, the son of a lace manufa On leaving school at 15 he at first helped his and was later apprenticed to a lithographer with acquired skill in draughtsmanship which proved in later life After another period in the lace tr

dinburgh at the age of 27 to study medicine ecame attracted to pathology At Edinburgh ich influenced by a fellow student W E Gye D Bullock) who came from the same part of After two years of clinical medicine he was for military service in the first world war At the war an educational grant enabled him to in pathology under Shaw Dunn
ed the scientific staff of the Medical Research 1920 and worked with Gye on the poisonous of colloidal silica they published three papers Then after some work on measles yielding esults, Purdy joined in Gye s work on fowl In 1925 Gye and Barnard published their the aetiology of tumours in this Gye main at for transmission of fowl tumours with o factors were necessary a non-specific virus ecific factor derived from cells there were ications concerning the aetiology of cancer in Work supporting this theory was published in book, *The Cause of Cancer* by Gye and Purdy t 17 years until 1942 Purdy worked with st the theory largely by immunological tech d by himself he published several papers on the on of fowl tumours in ducks Purdy was to ry loyal colleague and not a little of a hero r His work was most meticulous and every xamined most critically His careful drawings s were a great asset in his published papers
Gye became director of the Imperial Cancer Fund Laboratories, Purdy, still a member of al Research Council staff, was seconded to him On his retirement in 1942 he went to linical pathology at Beverley in Yorkshire and 946 helped to build up a pathological depart he Margate and District General Hospital
rdy was of a retiring disposition and rarely meetings. He was helpful and friendly to all him; and even those who disagreed with his out cancer had a high regard for his qualities rived by his wife

JOHN HENRY BADCOCK
F R C.S. F.D.S

dcock was 80 years of age when he died at on Sept. 28 Inevitably most of his coevals leceased him but many of a younger genera n a position to appreciate his services to the ofession.
eived his professional education at the Royal d Charing Cross Hospitals, and obtained the ions of L.D.S in 1887 and M.R.C.S in 1890 In y a year after qualifying in medicine he was l an assistant dental surgeon at Guy's Hospital 895 he became dental surgeon In 1898 he had le lecturer in operative dental surgery and in n with this lectureship he introduced the subthodontics, in which throughout his professional ok the deepest interest.
4 to the great regret of both his colleagues lents, Badcock resigned from Guy s Hospital ewhat sudden step which there is reason to e afterwards regretted Nevertheless he found scope in connection with his profession apart al practice and he used it to the full He was associated with the affairs of the British Dental on of which he had been elected a member in d he served as its treasurer from 1910 to 1924 ident in 1925 His interest in orthodontics led to the foundation of the British Society for the Orthodontics of which he was the first president 931 he presided over the second International tic Congress. His work in dentistry was d by the Royal College of Surgeons when it im to the fellowship in 1932 and to the fellow he Faculty of Dental Surgery on its institution. other distinctions he became president of the gical section of the Royal Society of Medicine and examinerships and many other appointments o make his life an extremely busy one
ck was a notable teacher and was prodigal of hich either he or others brought to fruition s example was the well known Badcock screw—as familiar in orthodontics as the Spencer Wells forceps in general surgery A man of considerable intellectual powers he loved beautiful things and enjoyed outdoor pursuits such as walking, climbing and boating He had great charm was quiet and gentle in manner, and was kind and helpful to a degree His teaching and example influenced and will continue to influence, many who knew him

JOHN VINCENT FORREST
C.B., C.M G., M B Edin.

Colonel Forrest who died at his Belfast home on Oct 10 will be chiefly remembered in Ulster for his association with the Royal Victoria Hospital Belfast of which he was medical superintendent from 1920 till 1930 His success in this office owed much, however to his previous wide experience and distinguished career

Born in 1873 he was the son of the late Mr William Forrest a member of the Legislative Council of Antigua in the Leeward Islands. He studied medicine at Edinburgh University and after qualifying M.B in 1894 joined the Army Medical Services He served both in the South African war and in the first world war In the 1914–18 war he served first on the staff of the D D.M.S at Boulogne and in 1917 he was appointed D D.M.S to the Italian Expeditionary Force For his services he was appointed C M G in 1916, and C.B in 1919 and he was six times mentioned in despatches

It was with this solid achievement behind him that he started in 1920 his ten years work at the Royal Victoria Hospital, with all the problems presented by a continually expanding institution These were days when paper counted much less than personality and when administration by its very elasticity and lack of tabulated regulations made the character and judgment of those responsible vitally important His great experience and sound judgment, together with a quiet but persuasive way with his lay and medical colleagues, levelled out many an obstacle On his retirement in 1930 the management committee and staff paid a tribute to his services by a donation to the building fund of the new maternity hospital and nominated him as a life governor

Colonel Forrest is survived by his wife with a son and a daughter

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Appointments

FOXELL, CAROL, M.B. Lond., D C.H asst. M O public-health department, London County Council
GOODDY WILLIAM M.D Lond., F.R.C.P honorary consultant neurologist, The Italian Hospital London
TOMKINSON, J S., M B. Birm, F.R.C.S. M.R.C.O G : part-time asst. obstetric surgeon, Guy's Hospital, London.
WILLIAMS, R. J M.A. Camb., F.R.C.S. : consultant surgeon Merthyr and Aberdare H.M.C.

The Hospital for Sick Children Great Ormond Street London :
CANDY JOSEPHINE, M.B. Wales resident anaesthetic registrar
LOCKHART-MUMMERY H E., M CHIR. Camb. F R.C.S : part time senior surgical registrar
MACKAY MARIA M B. Manc junior resident anaesthetist.
PALLOT DOREEN, M B. Lond., D.A resident anaesthetic registrar
ROTHFIELD N J., M.B. Sydney D C H. house physician.

Liverpool Regional Hospital Board :
CADMAN E. F B, M.D Wash. Univ., St Louis M.R.C.P D.C.H. part time visiting consultant physician hospital in the Southport area.
CARMICHAEL, J H F M.D Lpool. D.M R.D asst radiologist East Liverpool area.
McCARTY A G M.D Glasg D.M.R.D : consultant radiologist East Liverpool area.

Newcastle Regional Hospital Board :
BUTTERWORTH H C. M.B. Durh., D.A consultant anaesthetist Darlington H.M.C. group
CRAIGEN W G C., M B. Aberd. asst. ophthalmologist (S.H.M O) Sunderland H.M C.
EVERITT ELIZABETH M B Lond D A consultant anaesthetist Sedgefield General Hospital.
KEMSEY E L., M.B. Lond. F R.C.S consultant surgeon Sunderland H.M.C group

South Western Regional Hospital Board :
CROSS E. G W., M.R.C.S. D P.M : asst physician in psychiatry Bristol mental hospitals.
HOFFMAN J N., M.B. Lond. asst chest physician, Bristol clinical area.
LUKIANOWICZ, NARCYZ, M D Lwow asst. physician in psychiatry Bristol mental hospitals

Notes and News

CLINICAL RESEARCH AT THE MIDDLESEX

THE new Institute of Clinical Research, which was opened is week as a part of the Middlesex Hospital Medical School, ll provide a vantage point to which the clinician may with aw for a spell to consolidate and develop the ideas which ve sprung from his day to day work and which he has rhaps had to put aside for want of time or means to investi te them further The board of governors of the hospital ve decided to devote a considerable proportion of the spital's endowment fund to research, and, with the new stitute in mind, they bought a modern four storey building, nich had been used as a boys' club, a few minutes' walk from e hospital, so those who are fortunate enough to work in e agreeable surroundings that have now been prepared ere will be in fact detached, but not too remotely, from the isy hospital scene

The hospital's clinical research committee will allot grants om the income of the endowment fund to individual search-workers, who will then take their place in the institute r a prescribed term Each will be sponsored by one of the ddlesex consultants, who will supervise progress, but ose who receive grants need not necessarily be members of e hospital staff The equipment and laboratories of the stitute will be at their disposal, but any additional apparatus at they need will have to be paid for from their grant or om other grants that they may hold

The ground floor of the building is mainly taken up by six mfortable consulting rooms where patients, chosen for vestigation and follow up in a particular piece of research, ay be interviewed and examined These rooms include one rge one where a number of people can be dealt with at the me time, the plan is to use this room not only for patients it for students or other volunteers who are being used as sub ts for an experiment No great number of patients will be in e institute at any one time, so only a small (but handsomely rnished) waiting room has been provided On the first floor ere is a common room for informal gatherings of the staff d for occasional scientific meetings Then there are rooms different sizes for the research workers, so that each may ve a place to call his own The basic furnishings of these oms are simply a desk and a small laboratory bench, the cupant fills in the details

By no means all the doctors in the institute will deal rectly with patients, for clinical research is to be interpreted ry broadly as research by clinicians Some may need no ore than one of the smaller rooms on the first floor where ey can install their equipment and get straight to work on eir chosen problem Others will make many calls on the ochemical and pathological laboratories on the floor above tached to the biochemical laboratory is a measuring room using precision instruments The two laboratories will be the immediate charge of technicians from the corresponding partments of the hospital and they will keep in close touch th the parent laboratory A particularly useful feature of e third floor is the workroom where apparatus can be made modified to meet a special need, clearly, it is a much eaper proposition to adapt standard equipment to do the b in hand rather than call on the manufacturers to make a w instrument Demands on the workroom are expected be heavy On the top floor there is accommodation for boratory animals, with a roomy run for the dogs on the roof ray plant is installed in the basement in the ordinary way us will be used to examine those animals whose response to experiment can be judged radiologically, but a generous ansformer has been selected which can supply any kind of -ray tube that may be brought by someone doing research at is predominantly radiological

The institute, which is under the direction of Prof Alan ekwick, strikes out on a new and promising line For one ing it will give opportunities for a more deliberate and etter planned approach to clinical research, and, for another, will help to emphasise to newcomers the importance of ving a full explanation to the patients who have been vited to take part in a research inquiry

PREVENTION OF BARBITURATE POISONING

IN the *British Medical Journal* of June 13, 1953 (p 1335), r E Mackernan suggested that, to prevent deaths from verdose of a barbiturate drug each tablet should contain small amount of ipecacuanha which would act as an emetic when too many tablets were taken. British F Proprietaries (Middle Street, Taunton, Somerset) inform that they produce a range of standard barbiturates " safe in this manner" They say

> "Our experimental trials have shown that it is possible quantity of emetic in the form of the alkaloids of which has no significant pharmacological activity when quantities of tablets are used On the other hand, if an is taken an emetic dose is obtained before the barbiturate reaches lethal amounts. Moreover the action of emetic, which is due to direct gastric irritation, is prompt to ensure the elimination of the bulk of the barb before absorption occurs."

DANGEROUS DRUGS ACT

THE Home Office has issued an order[1] which part III of the Dangerous Drugs Act, 1951, to N morphine (the approved name is nalorphine) From Nov this drug will come within the provisions of the Act and regulations made thereunder

NEW MATERNITY BENEFITS

THE new maternity benefits,[2] introduced by the Nat Insurance Act, 1953, will be available to mothers babies are born on or after Monday, Oct 26 The new b are

Maternity grant of £9 for each baby born. This replaces present maternity grant of £4 and attendance allowance of £1 week for four weeks. The attendance allowance has been

Home confinement grant of £3 for mothers whose babies are at home or elsewhere than in a hospital or institution *tenance is paid for from public funds* This is an entirely new

Maternity allowance of £1 12*s* 6*d* for eighteen weeks fo in paid work and paying full national insurance during the year starting 15 months before the baby is born allowance (total £20 5*s*) replaces the present allowance of £1 for thirteen weeks (total £23 8*s*) paid at present to women paid work.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE

THE President of this society for the session 1953-5 Dr F NORMAN WHITE, whose distinguished career began the Indian Medical Service and included a long period in Health Organisation of the League of Nations and in School of Hygiene in Athens In his presidential Oct 15 Dr White recalled some of his experiences of major epidemic diseases, of which the first was the p of influenza that attacked Europe in the spring and of 1918, and in the autumn swept through India, where of the monsoon had already caused hardship through shortages Nowhere in the world was the epidemic so as in India, and in two months it caused 6 million there Rural areas suffered more than towns, and the was especially severe on young people By November, the epidemic was over, but Dr White, who during this was doing the work of the sanitary commissioner of government of India, and upon whom lay most of responsibility for coping with the emergency, showed had been a tragedy the magnitude of which was not appreciated by those living outside India

He went on to recall the great outbreak of typhus relapsing fever which, in 1920, spread from Russia to P and the neighbouring countries and which came as a immediate threat to war-devastated Europe Dr had been invited to take charge of an international ep commission set up by the council of the League of Na and in the autumn of that year he left for Poland with then the director of the State Serum Institute in Copen and Pottevin, of the Office International d'Hygiène P Conditions were appalling, there was typhus in every sometimes in every house, and refugee trains brought victims, alive and dead Relapsing fever and cholera to the miseries of these disorganised countries, and the preventive measures were few and called for much labo organisation Dr White mentioned some of the great who directed the relief organisations—Nansen, Rajchman Poland, and Tarassevitch of Russia—and he paid trib the Russian doctors and nurses who worked at such de risk to themselves in apparently hopeless circum

In 1922 the League of Nations sent Dr White on a to the Far East, where he met a number of out personalities, such as Shiga and Yersin, the discoverer of plague bacillus This tour led him to suggest the cre an epidemiological intelligence bureau at Singapore, un direction of the League of Nations. The bureau was

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[1] The Dangerous Drugs Act, 1951 (Application) Order, 1953 1953 no 1453 H M. Stationery Office 2*d*

[2] See *Lancet*, 1953, i 634

1923 and still remains active to demonstrate by its ermanent value the foresight of its founder

Dr White s story was one of great events dealt with uurageously in days when insecticides and antibiotics were nknown and when epidemics were terrible in their sweep and ower He spoke warmly of the able men who responded to ae challenge of these formidable diseases and though r White put a modest estimate on his own part in the attle, it was clearly a very important one

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Iniversity of London

At recent examinations the following were successful:

D.C.P.—J B. Adamson J D Arneaud M. C Berenbaum , R. Chapman, Siri Krishen Chopra Manoranjan Datta, B R avis, N U C Godfrey W F Hunter Samrit Jatinandana C. March Mary Ralston, W A Russell, M. P K. Shoobridge C. Squires H J Woodliff

D.P.H.—P P M Browne James Clearkin, K. A Rahman, T Subramaniam D R Thomson David Ungar

D.T.M. & H.—Paja Sirivorasarn

cottish Conjoint Board

At recent examinations for the diploma of licentiate of the oyal Colleges of Physicians and Surgeons of Edinburgh, and he Royal Faculty of Physicians and Surgeons of Glasgow he following were successful

J. A. Childs J C Douglas Ellis Hanford Santosh Khosla, J McA. Kirby G D B. Lindsay Patrick Murray Marie J ilbchester Mohammad Hasan Rizvi W J Ross, R. MacG Wight.

oyal College of Obstetricians and Gynæcologists

At the annual dinner of the college held in London n Oct. 16 the President Mr A. A. Gemmell referred to some f the college s plans. Next year was its silver jubilee and an ttractive programme in celebration was being arranged for he days July 13–15 when one of the functions would be ttended by Queen Elizabeth the Queen Mother The ollege museum continued to expand a steady flow of xhibits was coming in and it was clear that the potential xisted to create one of the best museums of obstetrics and ynæcology in the world The library must still concentrate n acquiring historical works until the college had more oomy premises To enable the college to enlarge its quarters, nuch more money was needed, and it had been decided to eopen the appeal fund next year with a new building as the bjective Sir Ronald Weeks would preside over the appeal Ir Gemmell was replying to the toast of The College pro osed by Sir Francis Walshe F.R.S Prof J F Cunningham elcomed the guests who as Mr Iain Macleod Minister of Health, observed in his reply considerably outnumbered the osts Mr Macleod hoped that Sir Ronald would let him now if there was any way in which he could help directly or ndirectly in the work of the college s appeal for funds. A istinguished visitor from the Commonwealth Sir Edmund Herring, lieutenant-governor of Victoria, also replied in riendly terms for the guests. He would he said like to ee more people from Great Britain making the journey o Commonwealth countries to see what the inhabitants were ike and how they lived; he felt sure that two-way traffic was one of the best ways of drawing together the Common wealth family

At a meeting of the council on Oct 16, with Mr Gemmell n the chair the following were admitted to membership:

L. J Abramowitz, Subrahmanyan Alankaram, W J R. Anderson . S Andrew, A K. Bose J C Brace T J Buckley, Samuel Burke . K. Burt, J G Cameron, R. S Casement, P W Christina Chow Maureen D Connolly, R. L. Edwards M B Flanagan F M C. oster Kathleen M. Frith, M C. G Grant, P B Guastalla, R. H J amlin, J. W S. Harris, J M Holmes, C A Jones, R. L Jones, R. Macdonald, Betty Mallace, G A Manly D N Menzies, M C. Hobelow J J Nattrass, H H Neifeld, F N Neser, J P. O Dwyer R. Patnaik, Clara Phillips, B G Pickles, William Rotheram S. Scott, J M. Stewart, R. A. Struthers, Valerie M. Thompson J Thornberry Harry Ulman C G Wilson.

oyal Sanitary Institute

At a meeting to be held in the town hall St Helens, at 0.30 A.M on Thursday Nov 5 Mr M Ward will read a aper on Sewerage Problems in Subsiding Areas and Dr G Brien and Mr D W Richardson will speak on Acquisition nd Modernisation of a Common Lodging House At 2 30 P.M n Wednesday Nov 11 Mr F T Wilkins, PH D will open discussion at the institute 90 Buckingham Palace Road ondon S.W 1 on Air Pollution and the London Fog of ecember 1952. An exhibition on smoke and smog will be pened on Monday Nov 9 in the museum of hygiene at the nstitute The exhibition will remain open until Dec 5

Royal College of Surgeons of England

On Oct 20 H.R.H the Duke of Edinburgh was admitted to honorary fellowship of the college

Mr Geoffrey Keynes will deliver the Cecil Joll lecture on Thursday Nov 12 at 5 P.M., at the college Lincoln s Inn Fields, London W C.2 He will speak on Investigations into Thymic Disease and Tumour Formation. Sir Reginald Watson-Jones will deliver the Bradshaw lecture on Wednesday Dec 9 at 4 P.M., at the college. His subject will be Fracture Treatment in the Next Half Century On Thursday Dec. 10 at 5 P.M Mr St. J D Buxton will deliver the Robert Jones lecture He will speak on Arthroplasty

Faculty of Anæsthetists—Dr Frankis T Evans will deliver the Frederic Hewitt lecture at the college, Lincoln's Inn Fields London, W C.2, on Friday Oct 30 at 4.30 P.M. He will speak on Freedoms of Anæsthesia.

Royal College of Physicians of London

On Oct 16 the Bisset Hawkins medal was presented to Dr W N Pickles, of Aysgarth. The citation ended as follows

> "As a student of epidemiology he stands in the forefront. But perhaps his outstanding achievement is the demonstration that scientific observation and deduction is not only possible under the pressure of a busy general practice but is a constant stimulus to the quality of the service that the general practitioner can give to his patients."

Renal Association

At a meeting of this association to be held on Wednesday Oct. 28 at the Ciba Foundation, 41 Portland Place London, W 1 at 4 30 P.M. Prof E. B Verney F.R.S Dr B E Miles, and Dr A. A. G Lewis will open a discussion on Emotion and Renal Function.

Bathing pool for Paralysed Patients

An anonymous gift of £5000 to provide a bathing pool at King Edward VII Hospital, Sheffield for the treatment of patients paralysed by poliomyelitis has been made to Sheffield Regional Hospital Board. Earlier this year it was decided that a new physiotherapy department would be provided, but that a pool would have to wait until there was more capital

Charing Cross Hospital Dinner

The annual dinner held in London on Oct. 10 was attended by well over 200 members of the staff and past and present students. Dr C M. Scott, proposing The Medical School spoke of its progress and of the happy atmosphere which always animated staff and students. Dr E. C Warner the dean, said that the school was again able to accept 1st M.B students and thus covered the whole course for medical degrees The facilities for clinical instruction had been extended by providing special demonstrations at the Queen Elizabeth Hospital for Children, by arranging for domiciliary midwifery and by enabling students to live and study for three weeks in the homes of general practitioners. He mentioned that in the past three years five former students had obtained the degree of master of surgery—a number greater than had been attained by any other school. Mr David Trevor proposed the health of Mr Norman Lake, the retiring senior surgeon, and of Dr H. W C. Vines, who is retiring from the chair of morbid anatomy Mr Lake he said had been connected with the school since he entered as a student in 1906 and had been senior surgeon for over twenty years—a period believed to be longer than that of any of his pre decessors; in addition to his distinction as a surgeon, he was a scientist of repute and an engineer of considerable skill. Professor Vines, as dean in the years following the late war had had the very responsible task of rebuilding the school, and he had been able to bring the departments of anatomy and physiology back to Charing Cross. Subsequently he had been chairman of the planning committee which had got as far as setting out detailed working plans of the new hospital and medical school Mr Lake and Professor Vines, in reply to the toast, made speeches which will long be remembered by those who were present. On behalf of the staff and students, Lord Inman, who presided made presentations to Mr Lake and Professor Vines. Of the funds collected the greater proportion will be used to establish a Norman Lake prize in final year surgery and a Prof H. W C Vines prize in pathology

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In our advertisement columns this week application is invited for a post as junior assistant editor of *The Lancet*

Royal Society of Medicine

On Oct 16, Mr A. T Glenny, F R S, received the Jenner medal for his outstanding contribution to the prevention and control of epidemic diseases, notably diphtheria

Empire Rheumatism Council

Dr Otto Steinbrocker (New York) will be the guest lecturer in the council's weekend course to be held at the Arthur Stanley Institute, Peto Place, Marylebone Road, London, N W 1, on Nov 13 and 14

Reciprocal Social Security

A reciprocal agreement on social security between the United Kingdom and the Grand Duchy of Luxembourg was signed on Oct 13 The agreement will enable national insurance pensions and industrial injuries benefits to be paid in Luxembourg, while the corresponding benefits of the Luxembourg social insurance schemes will become payable in the United Kingdom Moreover, national insurance contributions paid in both countries will be taken into account for the purpose of benefits in either country The agreement, which is subject to ratification, is expected to come into operation next summer

British Medical Students' Association

This association is holding its annual general meeting Nov 5 to 7 in Bristol The annual ball will be held on Frid Nov 6 Further particulars may be had from D I. D Ho c/o M C R, Royal Infirmary, Bristol

Congrès International de Médicine Sportive

The tenth international congress of medicine as applied sport will be held in Belgrade on May 19–22, 1954 details may be obtained from the secretary general, Dr Smodlaka, Belgrade, Deligradska, 27, Yugoslavia.

Frenchay Hospital, Bristol

New operating-theatres and extensions to the department of neurological surgery at Frenchay Hospital opened by Sir Geoffrey Jefferson, F R.S, on Oct The two new theatres will more than double the operating capacity, and the neurosurgeons will be placed to deal with an emergency case which arrives long elective operation is in progress The theatres air conditioned and equipped with pressure steam sterili The department is the base for the neurological service of the South-western Hospital Region

Diary of the Week

OCT 25 TO 31

Monday, 26th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W 12
4 P.M Dr C C Ungley Rôle of Vitamin B_{12} and other Hæmopoietic Factors in Megaloblastic Anæmias
UNIVERSITY OF LONDON
5 30 P M (London School of Hygiene and Tropical Medicine, Keppel Street, W C 1) Dr Paul F Russell (Rockefeller Foundation) Man's Mastery of Malaria—the Unfolding of Malaria Ætiology (First of five Heath Clark lectures)
ROYAL SOCIETY OF MEDICINE 1, Wimpole Street, W 1
5 30 P M *Section of Odontology* Mr Arthur Bulleid The Microbe Hunters (Presidential address)
ROYAL EYE HOSPITAL, St. George's Circus, S E 1
5 30 P M Miss J M Dollar Management of Cataract
INSTITUTE OF CHILD HEALTH, Hospital for Sick Children, Great Ormond Street, W C 1
6 P.M. Prof E Husfeldt (Copenhagen) Hiatus Hernia in Adults and Children (Alex Simpson Smith lecture)
MEDICAL SOCIETY OF LONDON 11 Chandos Street, W 1
8 30 P.M Mr H J Seddon Dr W Ritchie Russell Treatment of Early Stages of Poliomyelitis
MANCHESTER MEDICAL SOCIETY
5 P M (Dental Hospital University of Manchester) *Section of Odontology* Mr Colin Cooke Dentistry and the Social Services (Presidential address)
9 P.M (Medical School University of Manchester) *Section of General Practice* Dr R W Fairbrother Problems of Antibiotic Treatment in General Practice

Tuesday, 27th

UNIVERSITY OF LONDON
5 30 P.M (London School of Hygiene and Tropical Medicine) Dr Russell The Unravelling of Malaria Therapy (Second of five Heath Clark lectures)
6 P M (Birkbeck College Malet Street W C 1) Prof. W S Bullough PH.D History of Hormones
ROYAL SOCIETY OF MEDICINE
5 30 P M *Section of Experimental Medicine* Dr Audrey Smith Dr J E Lovelock, Prof P B Medawar F R S Dr P L Mollison Survival of Tissues at Low Temperatures
8 P M *Section of Medicine* Sir Henry Cohen Evolution of Concept of Disease (Presidential address)
INSTITUTE OF DERMATOLOGY St John s Hospital Lisle Street W C 2
5 30 P.M Dr S C Gold Allergy in Diseases of the Skin
MANCHESTER MEDICAL SOCIETY
4 30 P M (Medical School University of Manchester) Mr R L Newell History of Urinary Calculi
WEST END HOSPITAL FOR NERVOUS DISEASES
5 30 P.M (40 Marylebone Lane W 1) Minton Ocular Manifestations in Nervous Diseases

Wednesday, 28th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M Prof G F Marrian F R.S Steroid Metabolism (First of three lectures)
UNIVERSITY OF LONDON
5 30 P M (London School of Hygiene and Tropical Medicine) Dr Russell Development of Malaria Prophylaxis (Third of five Heath Clark lectures)
ROYAL SOCIETY OF MEDICINE
5 P M *Section of Endocrinology* Dr Raymond Greene Place of Endocrinology in General Medicine and Surgery (Presidential address)
ROYAL EYE HOSPITAL
8 P M Mr B H Dawson Blood supply of Visual Pathway and its Clinical Aspects
INSTITUTE OF DERMATOLOGY
5.30 P.M Dr J O Oliver Immunology
INSTITUTE OF UROLOGY, 10, Henrietta Street, Covent Garden, W.C
5 P.M Mr H G Hanley Urological Problems in
RENAL ASSOCIATION
4 30 P M (41, Portland Place, W 1) Prof E B Verney, Dr B F Miles, Dr A A. G Lewis Emotion and Function

Thursday, 29th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W C
5 P.M Sir Ernest Finch The Forerunner (Thomas lecture)
POSTGRADUATE MEDICAL SCHOOL OF LONDON
3 30 P M Professor Marrian Steroid Metabolism. (Second of three lectures)
UNIVERSITY OF LONDON
5 30 P M. (London School of Hygiene and Tropical Dr Russell Some International Aspects of (Fourth of five Heath Clark lectures)
INSTITUTE OF CHILD HEALTH AND INSTITUTE OF NEUROLOGY
5 30 P M (National Hospital, Queen Square, W C 1) Dr Sandifer Paralyses of Cerebral Origin in Early Cerebral Diplegia—Clinical Types, Diagnosis and ment
INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
3 P M (Chelsea Hospital for Women Dovehouse Street, S W Mr A A Gemmell Myomectomy
INSTITUTE OF DERMATOLOGY
5 30 P M Dr R W Riddell Diagnosis of Skin Infections Pathogenic Fungi
CIBA FOUNDATION
5 P M (1, Wimpole Street, W 1) Prof A von Muralt Neurophysiology Old and New Facts and (Ciba Foundation lecture)
MANCHESTER MEDICAL SOCIETY
8 P M *Section of Anæsthetics* Dr H E Pooler Child (Presidential address)
HONYMAN GILLESPIE LECTURE
5 P M (University New Buildings Teviot Place, Edin Dr Gordon O Horne Effects of Environmental

Friday, 30th

ROYAL COLLEGE OF SURGEONS
4 30 P M Dr Frankis Evans Freedoms of Anæst (Frederic Hewitt lecture)
POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P M Professor Marrian Steroid Metabolism (Last of lectures)
UNIVERSITY OF LONDON
5 30 P M (London School of Hygiene and Tropical Med Dr Russell Malaria and Society (Last of five Clark lectures)
ROYAL EYE HOSPITAL
4 30 P.M Mr A J Cameron Recent Advances in C Surgery
INSTITUTE OF DERMATOLOGY
5 30 P.M Dr Gold Skin Testing
MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES, Chandos Street, W 1
7 30 P M Dr E M C Dunlop, Mr F B Zwink Corneal in Congenital Syphilis

Births, Marriages, and Deaths

BIRTHS

EVANS —On Oct 9 at Fort Jameson, Northern Rhodesia to (née Thornton) wife of Dr A. J Evans—a son

MARRIAGES

BATES—HUTCHESON —On Sept 24, in London Josh Lyon M B M R.C.P, D P.M, of Borocourt, near Reading to Edythe Hutcheson, daughter of Dr and Mrs Wm. H of Teignmouth, Devon

OCIOMEDICAL ASPECTS OF DIABETES MELLITUS *

R E TUNBRIDGE
O B.E M.D M.Sc. Leeds, F.R C.P
PROFESSOR OF MEDICINE, UNIVERSITY OF LEEDS

DIABETES mellitus is one of the commonest medical orders In this country today there are about 150,000 own diabetics, and probably there are a similar number yet undetected. More than half of all diabetics are over age of 40 and the proportion of the population over is rapidly increasing; thus within twenty years this ntry is likely to have at least half a million diabetics nearly 1% of the population The treatment of betes mellitus therefore is a national as well as an dividual problem.

Diagnosis and Detection

Beaser (1948) analysed the early symptoms of all tients attending a diabetic clinic, and found that 34% d classical presenting symptoms, and altogether 77% mptoms suggestive of diabetes mellitus Diabetic mplications were a presenting feature in only 19%, d weight loss was noted initially in less than half the tients. Beaser remarks that the severity of diabetes ellitus measured by the patient's insulin requirement, influenced by the following factors, named in order importance: (1) a period of untreated glycosuria) metabolic decompensation, (3) age. A large proportion the adult patients were found to have had glycosuria r anything up to sixteen years before they came under eatment, and 80% had a history of glycosuria for at ast two years before receiving treatment. Simon (1953) a survey of diabetics living in the eastern health district Baltimore confirms this experience; for only 8% had d diabetes diagnosed early, compared with 78% in om it was diagnosed late

The so-called complications are the most important nical problems in diabetes mellitus, and their onset is lated to the duration of the disease Thus it is essential know whether adequate control of the diabetes fluences in any way the incidence of complications e Joslin school (1952) hold that poor control increases e liability to complications, but their results relate to e treatment of patients once the diagnosis has been ablished. Rabinowitch (1949) followed up for ten ars a series of private patients who had presented tially with glycosuria and some slight abnormality the glucose-tolerance test, such as an abnormal peak a lag type of curve, but who had had a normal fasting od-sugar and a normal blood-sugar two and a half urs after a meal. In all, 133 patients were studied; had been kept on diets as a precautionary measure, ile 49 had either not been dieted or else had soon carded dietary control and were therefore not included the dieted group The incidence of frank diabetes was ch higher in the group that had not been dieted Of series as a whole 39 (29 3%) developed frank diabetes incidence was higher in the patients with a family tory of diabetes mellitus This study for the first time vided evidence that precautionary dietary treatment the doubtful case lowered the risk of frank diabetes, it thus enhanced the importance of the detection ves in which the American Diabetic Association has aged for the last five years

The pioneer survey of Wilkerson and Krall in 1947 made at Oxford Mass. where of a population of 3 they examined the urine and blood of 3510—just r 70% of the inhabitants They used Benedict's test for the urine analysis, and capillary blood for the blood-sugar estimation They found 70 cases of diabetes mellitus 40 previously recognised and 30 new cases. The later surveys in Arizona (Joslin 1940) Brooklyn (Hartweg and Glenn 1951), Jacksonville (Ford 1949) Dayton (Sharkey et al 1950), St. Louis (McBryde 1949, Olmsted et al 1953), Gloucester, Mass (Getting et al. 1952) and in Canada (Kenny and Clute 1951, 1953) have all indicated that approximately one new case of frank diabetes is discovered for every one previously known

In the early survey at St Louis the urine samples were collected in bottles which were obtainable from pharmacists This method had obvious difficulties connected with preservation of specimens and collecting packing and sterilising of the containers A later suggestion that the pharmacist should test the sample of the urine was not acceptable to the public. For later surveys Drey (1950) worked out two new devices the Drey pack' and a simpler modification which should be of inestimable value not only in survey work but possibly also in the routine follow up of patients attending clinics In surveys true diabetes is commonly brought to light by the discovery of severe glycosuria Urine testing is especially valuable because of its simplicity but blood sugar estimation is more reliable if only a single test is to be used.

The Gloucester survey (Getting et al. 1952) illustrated the difficulties of detection surveys and especially the problem of human caprice.

> In this survey self testing sets were distributed after intensive propaganda and the instructions for testing were very simple 3232 persons registered for the sets, 1730 did the test, 1181 failed to test and 341 could not be traced. Of those testing, 75% reported no difficulty with the test, and 8% difficulty; and 17% could not follow the instructions Among those failing to do the test the cause was lack of interest in 40% and difficulty over the test in 29%. Further analysis of the age and academic standing of those who failed to test showed no significant difference from those who succeeded.
>
> Still more disappointing was the fact that of the 98 including 13 known diabetics, who obtained a suspicious response only 23 consulted their physician as requested if the result was suspicious.

The Gloucester survey underlines four features of any detection drive: (1) the difficulty of maintaining interest (2) the procrastination in doing tests (3) the inaccurate interpretation of tests, despite simple instructions; and (4) the failure of persons with a suspicious test to obey instructions and report to their physician. Getting et al suggest that testing should be done centrally and the patients followed up individually where blood-sugar analysis is necessary In volunteers it is impossible always to get specimens at a certain fixed time after a meal. Hartweg and Glenn (1951) have reassessed the data from some of the surveys and consider the following values are significant for capillary blood:

Hours after breakfast	*Blood sugar (mg per 100 ml.)*
½–1½	160
1½–2½	150
2½–3½	140
3½+	130

They suggest that these are minimal figures, and that where they are reached or exceeded it is advisable to do a full glucose tolerance test Other methods of detection use less elaborate techniques. Ford (1949) followed up the relatives of diabetic patients immediately after diagnosis and found 31 cases amongst 736 people tested. The Boston Health Department distributed testing containers to 2000 patients who were attending for mass radiography examination 1133 of the containers were returned in 16 instances there was glycosuria of the 16 patients 8 were known and 8 unknown diabetics

Diabetic detection surveys are costly in time, man power and material and must be repeated frequently

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venth Banting memorial lecture of the British Diabetic Association, delivered at Leeds on July 17 1953

A further survey in Oxford, Mass, four years after the initial study, discovered new cases of diabetes mellitus not detected or suspected in the first survey (Joslin 1952)

All the surveys have nevertheless demonstrated frequency and importance of glycosuria Rabinowitch (1949) has also shown the importance of glycosuria as a herald of frank diabetes Whether detection drives, as recently organised in the United States, are the best method of discovering diabetes mellitus is still uncertain It is apparent that the profession needs to reorientate its views as to the significance of glycosuria, the need for blood sugar analysis, and the pitfalls in interpreting glucose tolerance findings, such as the danger of relying too much on fasting values and the importance of peak figures, lag curves, and the time of day when samples are taken

Treatment

The discovery of insulin revolutionised the attitude of both patients and doctors towards diabetes mellitus It is often said that nowadays patients die, not of, but with, diabetes mellitus Is this the whole truth? Despite more than thirty years' experience of insulin there remain many unsolved problems both as to its fundamental action and as to the best method of using it in individual cases

Rosenbuch (1945) asks "if the prognosis of diabetes in childhood—taking the long view—is, in spite of the progress of dietary and insulin treatment, more adverse than had originally been expected" Numerous reports (Dolger 1947, White and Waskow 1948, Root et al 1950, Larsson et al 1952) in recent years have emphasised the prevalence of the so called complications of diabetes mellitus—cardiovascular degeneration, hypertension, renal lesions, cataract, and retinal changes—and all have suggested that the onset of these is related to the duration of the disease Disagreement exists as to the part played by poor control in the causation of so-called complications, but there is general agreement that the most important factor is duration of the disease The evidence that cardiovascular and neuropathic complications are directly due to diabetes mellitus is not so sound as in the case of the more specific lesions—the aneurysmal dilatation of the vessels of the retina described by Ballantyne (Ballantyne and Loewenstein 1944, Ballantyne 1945) and the renal lesion described by Kimmelstiel and Wilson (1936)

I would emphasise that it is hardly justifiable to refer to the lesion described by Kimmelstiel and Wilson as a clinical syndrome The severity of the histological change seems to be related to the duration rather than to the severity of the diabetes, and although severe change is associated with albuminuria, hypertension, and retinitis, quite severe change is also found in diabetic patients who have died from non renal causes or accidentally. If these lesions are specific to diabetes mellitus, and proportional in severity to the duration of the diabetes mellitus, are they preventable? Are they less frequent in the well controlled diabetic? If so, what constitutes good control? And are the present methods and standards of treatment satisfactory?

WHAT IS GOOD CONTROL?

What constitutes good control? The greater freedom in therapy resulting from the introduction of insulin has tended to make physicians neglect earlier work and to be slow in applying physiological knowledge Allen and Sherrill said in 1922—and it is equally true today—"insulin has tremendously improved diabetic treatment but has not simplified it" Physiological and chemical evidence confirms the opinion of Allen (Allen and Sherrill 1922 Allen 1953) that dietary restriction, quite apart from its role in the prevention of obesity, is essential for good treatment. Houssay and Martinez (1947) found that in s which had undergone subtotal pancreatectomy the development of diabetes was accelerated by overfeedi Furthermore they showed that the composition of th diet within a fixed calorie intake had a variable eff A high-fat (lard) diet caused rapid development diabetes in all such rats, a high-carbohydrate d produced a similar but slower effect in all rats, when with a high protein diet only 75% of the rats becam diabetic Houssay and Martinez also compared th effects of giving the rats their food (*a*) in one meal a day and (*b*) divided into three meals Diabetes develop more rapidly in the animals fed once a day than in th fed three times a day Thus experimental work sugge that not only the total calorie intake but also composition of the diet is important

Kekwick (1952), treating obesity in diabetic and n non-diabetic patients, found that the composition of th diet as well as restriction of calories helped to determi the rate of weight loss

Stetten (1949) emphasised that in the diabetic anim the metabolism of carbohydrate, protein, and fat yiel compounds which can take part in the tricarboxylic ac cycle, so that interference with carbohydrate metabol may have repercussions on the metabolism of both p and fat Joslin's (1952) definition of diabetes mellit indicates clearly that the clinical syndrome of d mellitus has many possible ætiological factors, and th it is not always due to an absolute deficiency of insuli but may be due to a diminished effectiveness of ins secreted Considerable clinical, pathological, and expe mental evidence support his views Warren and LeComp (1952) found that in over a third of patients who h died with diabetes mellitus the pancreatic β cells and th islets of Langerhans appeared normal Wrenshall et a (1952) estimated at necropsy the insulin content of th pancreas in diabetic and non diabetic subjects and fou a lower average extractable insulin content in diabe subjects, in these the amount of extractable insu increased continuously with age from very low values i the young to approximately half normal values in the fifth decade That diabetes mellitus in man is not sim a matter of insulin deficiency is shown by compar of the insulin requirements of diabetic patients with th of patients who have had a total pancreatectomy f carcinoma of the pancreas The latter patients reta normal insulin sensitivity, and on liberal diets requ less than 50 units of insulin per day (Warren 1951)

Bornstein (1950a and b) and Willebrande et al (19 have recently described techniques for measuring th insulin content of blood, and have found considera reduction and variation in the blood insulin values patients with diabetes mellitus Even more striking is th report that the blood insulin values of patients with a initial level are rapidly restored to normal by treatme and that injected insulin does not per se increase the bloo insulin levels (Beaser 1952, Groen et al 1952) The findings, if confirmed, would suggest that once diabe mellitus is diagnosed vigorous treatment should be star immediately to restore the blood insulin values to norm in other words, insulin therapy should be begun at on even if this may not be required permanently

Soskin and Levine (1937) demonstrated that the r of sugar utilisation by the extrahepatic tissues var directly with the level of the blood sugar This confir the hypothesis of some clinicians that hyperglyc was not necessarily harmful, and that slow stabilisat first by diet and later, if necessary, by insulin, wit undue emphasis on normoglycæmia, was a sound met of treatment The experimental work of Dohan a Lukens (1947 1948), who produced persistent diab in cats by intraperitoneal injections of a glucose solut suggests that hyperglycæmia per se may be harm Many factors are concerned, however, in the regulati the blood sugar level, and alterations in this level not the only metabolic disturbances in diabetes

Reports on dietary control reveal striking differences in ractice (Lichtenstein 1944–45, Guest 1947, Tolstoi 1948, ilson et al. 1952). Mosenthal (1948) has divided the rotagonists into three groups—the purists, the middle f the-roaders, and the free-dieters. Beaser (1951), in n attempt to survey present methods of treatment, sent questionnaire to one in three of the medical members f the American Diabetic Association. 70% stated that ey aimed at normoglycæmia, and half of these physi ians also tried to obtain a sugar-free fasting urine. A rther 23% aimed at aglycosuria, and only 7% were not orried about glycosuria. All the physicians agreed that well-controlled diabetic should maintain an ideal eight and avoid obesity; that the diabetic should feel ell and fit, and should avoid both ketosis and hypo lycæmia. An analysis of the methods used to calculate he diets showed that the majority used a household erving technique, and that only 25% estimated the daily alorie needs by a formula. Beaser was in fact impressed y the similarity of the methods of treatment.

These findings go far to explain the fallacy of so many onclusions based on supposed dietary control. In eading published reports it is abundantly clear that one f the important factors in all therapy is the personality f the physician and the zeal with which treatment is dvocated by him and is followed by the patient. The rguments for and against the free diet are confused by eglect of these facts.

Forsyth et al. (1951) showed that of 50 patients on an nrestricted diet who were followed up for five years, 1 had to be put on to a controlled diet—in 2 cases ecause of the development of obesity, in 2 because of he development of hypoglycæmic reactions, and in 7 ecause of increased insulin requirements. In this short eriod of observation they found no proof that the develop ent of complications was related to the form of diet. ten-year follow-up from the Lichtenstein Clinic (Larsson t al. 1952) does not show any clear evidence in favour f the free, as opposed to the controlled diet. On the ther hand, the Joslin school (Joslin 1952) repeatedly tate that the incidence of complications is much lower n the well-controlled diabetic.

SURVEY AT LEEDS

With a view to analysing the ability of patients to aintain dietary control I undertook in the spring of 948 a survey of patients attending the Diabetic Clinic t the General Infirmary, Leeds. From a nominal roll of ll the patients living in Leeds and attending the clinic very fifth name was taken, making 103 in all. The atients were asked to keep a careful record of all meals or one week; and it was clearly explained to all taking art that the information was confidential. A social orker visited the home, first immediately before the urvey began, to assess home conditions and the economic osition, secondly during the week of the survey to check he record, and finally at the end of the survey to collect he results. In addition the patients kept an account f the money spent on food and in many cases gave full etails of family income. At the same time the cost of a iabetic diet was determined in four typical districts of eeds—the City Market, a new housing estate, a suburban rea, and one of the poorest parts of the city. The cost f an average diet corresponding to 14 Lawrence Black ines and 8 Red Lines was estimated both for the foods s purchased over the counter and also for the foods as n experienced caterer with good facilities for storage night purchase them. Of the 103 patients on the nominal oll 94 coöperated. The diets were analysed for food ontent, caloric value, correctness, and cost by Miss A. M. oyle, senior dietitian to the hospital, Dr. R. G. Paley, nd myself. Certain queries about household measures ere checked wherever possible, and where no such heck was possible the results were classified as unsatisfactory. It was found that the accuracy of the dietary treatment of the 94 patients was satisfactory in 16, moderately satisfactory in 44, and hopeless in 34. In the satisfactory group the variation in the calorie content from day to day was less than 15%, and in many cases it was of the order of only 5%. These results, I suggest, are probably no better or worse than those that would be obtained from many of the major clinics in this country or America, and they illustrate how liable to error are conclusions based on outpatient dietary control. It is very easy to maintain good dietary control for short periods in hospital, but it does not follow that a high percentage of those so easily controlled in hospital can maintain a satisfactory diet in their own homes.

Causes of Failure

Why do patients fail to maintain a satisfactory level of control? I suggest that this failure is due to three main groups of causes—psychological, social, and educational.

PSYCHOLOGICAL CAUSES

The psychological factor is especially prominent in the juvenile diabetic. In the pre-insulin days the problem seemed discouraging because the prognosis was so hopeless. Today, however, the position is different, and most clinicians will have experienced difficulty in stabilising the juvenile diabetic. Their reactions seem surprisingly different from those of children with other chronic diseases. The trauma caused by the discovery of diabetes appears to be deeper and more disturbing than the anxiety induced by other chronic diseases (Benedek 1948). It has been suggested that the disease is more prevalent in certain constitutional types (Daniels 1939); but Bruch (1949) in a report based on a study of 37 children showed that there was no uniform picture which characterised diabetics, in contrast to obese patients who showed a definite constitutional pattern. Herskovitz (1930) has, however, shown that in diabetes depression and hypochondriacal trends appear early, and an initial period of adjustment is necessary before making a psychological assessment. The psychiatric difficulties are much greater in the dependent type of individual, but the main problem is one of family adjustment, and psycho-analytical techniques are of little value. It is most important to evaluate the stability of the home, the marital relationships, the attitude to other children, and the special attitude of the child in relation to therapy. Unfortunately tolerance and understanding on the part of parents in the first few years is uncommon. Rather their attitude is one of self-pity ("What have I done to deserve this?"), rejection, or aggression combined with a perfectionist attitude ("I will not stand for it; if anything goes wrong it is not my fault"). The importance of these emotional conflicts is very clearly brought out by the work of Hinkle (Hinkle et al. 1951, Hinkle and Wolf 1952). He and his co-workers have shown that a stressful situation produces a fall in blood-sugar and the serum inorganic phosphate and a rise in ketonæmia, the effects being more distinct in the diabetic than the non-diabetic. They also recorded different responses in the postabsorptive state and following the injection of glucose. Situations leading to reactions of dejection, resentment, and loneliness were associated with higher and prolonged glucose-tolerance curves, whereas situations fraught with anxiety and tension might lead to a less elevated curve and were sometimes associated with relative hypoglycæmia in the third to fourth hour. These experimental studies have been applied both to the unstable, brittle diabetic and the elderly and relatively stable diabetic. Rosen and Lidz (1949) observed that in labile diabetics stressful situations were commonly associated with an exacerbation of the diabetes along with ketosis and coma. Likewise periods of relative security were associated with remissions, marked by reduced insulin requirements and a tendency to hypoglycæmia Over eating was shown to be a characteristic response to stress These findings help to explain the extreme instability of some juvenile diabetics Psychiatrists contend that insistence on a controlled diet is a very important factor in producing these situations, the child resenting both discipline—often aggressively imposed by the parent—and the fact that he is different from other children In consequence Mirsky (1948) and Benjamin (1947) have suggested that juvenile diabetics should be placed on a free diet It is interesting to compare this view with the findings of Forsyth et al (1951), who showed that a free diet failed to control adequately their juvenile and young diabetic patients but seemed more satisfactory with the older group What has been said about the juveniles applies equally to all diabetic patients The older patients, however, have learnt some degree of restraint, particularly of their emotions Even though they do not necessarily react so openly, their reaction may still be similar to that of younger patients, and the experimental work of Hinkle et al (1950) confirms this I think most would agree with Rosen and Lidz (1949) that with few disorders is it more clearly necessary for the physician to consider the patient's problems and idiosyncrasies Undoubtedly the erratic course of a number of diabetics is partly due to the patient's failure to adjust to the new situation, and partly to the physician's failure to realise the importance of this mental factor

SOCIAL CAUSES

The social impact of diabetes mellitus is equally neglected In the past diets were often prescribed in which four meals consisting of breakfast, lunch, dinner, and a supper snack were prescribed, without any recognition that few working class families had, even before the late war, two cooked meals a day Furthermore, often the foods prescribed were unfamiliar to the patients or beyond the range of their pocket The cost of a diabetic diet has, until recently, been overlooked.

In the survey that I undertook in 1948 (Tunbridge 1949) it was shown that the cost of a diabetic diet averaged about 23*s* per week (ranging from 15*s* 6*d* to 40*s*) in the group who were considered to have kept strictly to their diet The lowest figure (15*s* 6*d*) was the only one under a pound and was from a Scottish housewife with a big family and a very large kitchen-garden The average cost of 23*s* corresponded very closely to the figure of 21*s* 6*d* calculated as the proper cost by a dietitian and myself By comparison the cost of food for non-diabetic members of the families ranged from 8*s* to 16*s*, with an average of just over 10*s* Each year a similar costing has been made for the same standard diet, and the figure for the spring of this year was 34*s* The failure of many diabetics, particularly the elderly, to maintain a steady diet is undoubtedly due to financial stringency The influence of cost on the diet was also shown in the detailed analyses Usually on the first two or three days after pay day the diets were reasonably accurate, but from then on when funds did not permit the buying of extras the diet rapidly deteriorated to one of bread-and-butter and tea Other important social considerations were the lack of various utensils and of suitable accommodation for storing food A further important dietetic finding was protein deficiency in the lower income groups, this was usual unless the patient had been persuaded to take a pint of milk a day The very sound rationing policy of the Government during the war years, with the special rations for diabetics, undoubtedly enabled many diabetics to maintain a reasonably adequate diet For many patients the lessening of restrictions will no doubt complicate dietary care and control Since there is still no cure for diabetes mellitus, [illegible] patient's life has to be replanned.

EDUCATIONAL CAUSES

Practice often falls far short of theory, and there a few accounts, other than in handbooks, to indicate th methods of educating diabetics It is often forgotten th even a medical man, with a physiological training bef the onset of the disease, requires at least three months dietary control before he can enter a restaurant an order an accurate meal without undue emotional tensio If this is the minimum time required for the educationa and emotional adjustment of a trained subject, and on of good intelligence, how much more difficult it mu be for the ordinary patient Another important difficult in the elderly is that they are extremely loth to chang their habits It is comparatively easy to instruct a youn adult, but much more difficult to make a lady of change her way of life She has always done thing own way, and in any case food is one of the cen features of her life

In this country we are deeply indebted to Dr Lawren for his admirable books and for his work in coöperatio with Prof R A McCance, F R S, and Miss E Widdowson, D SC, in analysing common foods in ter of available rather than total carbohydrate content Many instructional books, mostly American, are no available, these are designed to suit all tastes, includin that for strip cartoons

It is only the exceptional patient who can ap the full significance of the carbohydrate, fat, and content of a diet If one can make the patient un the carbohydrate equivalents and the significance total calorie intake, reasonable dietary control can achieved To attain and maintain such a standard necessary to use every device possible—talks, discu displays, demonstrations, and films—with the cons repetition of essentials The physician must tak active part in such teaching He needs of cours assistance of trained staff—e g, dietitians, almoners, specially trained nurses—but they should all form team and take every opportunity to help the diabetic his problems The patient is far more likely to coöpe if the physician takes a personal interest in his diet makes a point of asking detailed questions relating dietary control as well as showing readiness to questions in detail

Should patients weigh all their food? Routinel more practicable to use household measures than s and reasonable accuracy can be attained with former Ideally a patient should, from time to check her diet by weighing the food It is regrett that adjustable scales, which are much in demand, not obtainable at a reasonable price in this count though such equipment is readily available in the Uni States

Environment

CAMPS

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Wherever possible, patients should be taught to administer their own insulin. Repeated demonstrations of the technique should be given, with ample opportunity for discussion Patients should bring their syringe and equipment with them to the clinic from time to time for routine overhaul Many difficulties would be solved by the adoption immediately of a standard syringe and the abolition within, say six months of all other varieties supplied to N H S patients

MARRIAGE

The mechanism of inheritance of diabetes mellitus is still not clearly understood, but it is generally accepted that a diabetic tendency can be inherited. Pincus and White (1933 1934) originally suggested that this tendency was inherited as a mendelian recessive but this view has not been accepted without reservation by later workers (Harris 1949 Watson and Thompson 1950) Certainly in juvenile diabetics there is considerable evidence for the hypothesis of Pincus and White, but one of the many difficulties in assessing diabetic inheritance is the variety of clinical syndromes which are labelled as diabetes mellitus and the possibility that clinical diabetes in the middle-aged is not the same disease as diabetes in the young From the point of view of inheritance however, it would seem unwise for a diabetic woman married to a diabetic man to have a family Far more important to the diabetic woman is the increased risk of toxæmia of pregnancy and of fœtal abnormality and mortality In recent years owing remissions, marked by reduced insulin requirements and a tendency to hypoglycæmia Over eating was shown to be a characteristic response to stress These findings help to explain the extreme instability of some juvenile diabetics Psychiatrists contend that insistence on a controlled diet is a very important factor in producing these situations, the child resenting both discipline—often aggressively imposed by the parent—and the fact that he is different from other children In consequence Mirsky (1948) and Benjamin (1947) have suggested that juvenile diabetics should be placed on a free diet It is interesting to compare this view with the findings of Forsyth et al (1951), who showed that a free diet failed to control adequately their juvenile and young diabetic patients but seemed more satisfactory with the older group What has been said about the juveniles applies equally to all diabetic patients The older patients, however, have learnt some degree of restraint, particularly of their emotions Even though they do not necessarily react so openly, their reaction may still be similar to that of younger patients, and the experimental work of Hinkle et al (1950) confirms this I think most would agree with Rosen and Lidz (1949) that with few disorders is it more clearly necessary for the physician to consider the patient's problems and idiosyncrasies Undoubtedly the erratic course of a number of diabetics is partly due to the patient's failure to adjust to the new situation, and partly to the physician's failure to realise the importance of this mental factor

SOCIAL CAUSES

The social impact of diabetes mellitus is equally eglected In the past diets were often prescribed in which four meals consisting of breakfast, lunch, dinner, and a supper snack were prescribed, without any recognition that few working class families had, even before the late war, two cooked meals a day Furthermore, often the foods prescribed were unfamiliar to the patients or beyond the range of their pocket The cost of a diabetic diet has, until recently, been overlooked

In the survey that I undertook in 1948 (Tunbridge 1949) it was shown that the cost of a diabetic diet averaged about 23*s* per week (ranging from 15*s* 6*d* to 40*s*) in the group who were considered to have kept strictly to their diet The lowest figure (15*s* 6*d*) was the only one under a pound and was from a Scottish housewife with a big family and a very large kitchen-garden The average cost of 23*s* corresponded very closely to the figure of 21*s* 6*d* calculated as the proper cost by a dietitian and myself By comparison the cost of food for non-diabetic members of the families ranged from 8*s* to 16*s*, with an average of just over 10*s* Each year a similar costing has been made for the same standard diet, and the figure for the spring of this year was 34*s* The failure of many diabetics, particularly the elderly, to maintain a steady diet is undoubtedly due to financial stringency The influence of cost on the diet was also shown in the detailed analyses Usually on the first two or three days after pay-day the diets were reasonably accurate, but from then on when funds did not permit the buying of extras the diet rapidly deteriorated to one of bread-and-butter and tea Other important social considerations were the lack of various utensils and of suitable accommodation for storing food A further important dietetic finding was protein deficiency in the lower income groups, this was usual unless the patient had been persuaded to take a pint of milk a day The very sound rationing policy of the Government during the war years, with the special rations for diabetics, undoubtedly enabled many diabetics to maintain a reasonably quate diet For many patients the lessening of tions will no doubt complicate dietary care and Since there is still no cure for diabetes mellitus, nt's life has to be replanned

EDUCATIONAL CAUSES

Practice often falls far short of theory, and there few accounts, other than in handbooks, to indicate methods of educating diabetics It is often forgotten th even a medical man, with a physiological training befo the onset of the disease, requires at least three months o dietary control before he can enter a restaurant a order an accurate meal without undue emotional tensio If this is the minimum time required for the edu and emotional adjustment of a trained subject, and of good intelligence, how much more difficult it mu be for the ordinary patient Another important diffic in the elderly is that they are extremely loth to cha their habits It is comparatively easy to instruct a you adult, but much more difficult to make a lady of change her way of life She has always done things own way, and in any case food is one of the centr features of her life

In this country we are deeply indebted to Dr Lawre for his admirable books and for his work in coöp with Prof R A McCance, F R S, and Miss E. Widdowson, D SC, in analysing common foods in ter of available rather than total carbohydrate Many instructional books, mostly American, are available, these are designed to suit all tastes, that for strip cartoons

It is only the exceptional patient who can apprec the full significance of the carbohydrate, fat, and content of a diet If one can make the patient unde the carbohydrate equivalents and the significance of total calorie intake, reasonable dietary control can be achieved To attain and maintain such a standar necessary to use every device possible—talks, discus displays, demonstrations, and films—with the con repetition of essentials The physician must tak active part in such teaching He needs of course assistance of trained staff—e g, dietitians, almoners, a specially trained nurses—but they should all form team and take every opportunity to help the diabetic wi his problems The patient is far more likely to coöpera if the physician takes a personal interest in his diet a makes a point of asking detailed questions relating dietary control as well as showing readiness to answ questions in detail

Should patients weigh all their food? Routinely it i more practicable to use household measures than scal and reasonable accuracy can be attained with the former Ideally a patient should, from time to tim check her diet by weighing the food It is regrettab that adjustable scales, which are much in demand, ar not obtainable at a reasonable price in this countr though such equipment is readily available in the Unit States

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INSURANCE

For many years it has been suggested to diabetic patients that their expectancy of life, if they maintain good control, does not fall far short of that of a normal individual Joslin was the first to preach this gospel, and in his enthusiasm went so far as to suggest that with the greater care diabetics exercised over their health their expectancy of life might be greater than normal Diabetic patients, however, were somewhat disconcerted by the attitude of the insurance companies, for, until 1940, these refused to consider a diabetic patient even at an enhanced premium In 1940 the Manufacturers Life Insurance Company of Canada first undertook life assurance for the diabetic A number of other companies have since adopted a similar policy, and in this country a diabetic can obtain insurance at an increased premium Blotner and Marble (1951), in discussing life assurance, laid down a number of points which they consider should decide the acceptability of a candidate—the age at onset of diabetes, the duration of diabetes, the prescribed diet and adherence to it, the insulin dosage and faithfulness in keeping to this, the frequency of urine tests for sugar and nature of the results, the common level of the blood-sugar, the incidence of coma and severe hypoglycæmic reactions, evidence of degenerative complications, chest radiographs and electrocardiographs, and how often the applicant attends his physician This list is formidable, and it would be interesting to know the relative importance attached by the insurance companies to each of these criteria Montgomery (1952), writing on his experiences with the insurance of diabetics, does not list so many factors but emphasises the importance of the conscientiousness with which the patient supervises his treatment and the regularity with which he attends his physician It is noteworthy that, although experience is limited, the insurance companies have so far shown no regret at having undertaken the insurance of diabetics In this country it is necessary for the diabetic to submit, in addition to the ordinary proposal form, a special diabetic questionnaire, and to give the name of the clinic he is attending and also that of his private doctor The diabetic questionnaire asks routine questions about diet, insulin, and duration of disease, but too much detail is not sought about blood sugar estimations and other points, although in the medical report all this essential information is required No specific question is asked about family history, and as far as I can judge the companies as yet attach no particular importance to family history in accepting or rejecting an applicant Similarly in this country radiographic examination of the chest is not demanded as a routine It is still early for a full actuarial assessment, but the fact that the insurance companies are not dissatisfied with their experience hitherto is reassuring for the diabetic patient, and also encouraging to those concerned in the supervision of patients

ASSOCIATIONS

This country, under the persuasive influence of Dr R D Lawrence was the first to form a diabetic association At first the project was much criticised, but the [illegible]e of such an association has been proved by the [illegible]r of similar associations founded in other countries, [illegible]nly for diabetics but also for patients with other chronic or crippling disorders Through the association members can keep up to date with current practice and thought, exchange ideas, and receive encourag without the need to declare publicly that they are su to the inconvenience of a diabetic life Success have their value in serving as a stimulus and encour ment to weaker brethren An association has also a in educating the public as well as the patient and medical profession, and it can make representations official bodies about matters, such as emplo driving licences, syringe manufacture, rationing, or foods, and insurance, which are so important to individual patient

RESPONSIBILITY FOR TREATMENT

It is estimated that in Great Britain today the 3 proved cases of diabetes mellitus per 1000 o population Joslin considers that for every k diabetic an undiagnosed case of diabetes exists, so one could assume that on the average in this countr general practitioner might be expected to have at l a dozen diabetic patients on his list at any one With this limited clinical material and the lack necessary facilities for blood sugar determination, practitioner cannot be expected to assume the responsibility for surveillance, although he should versed in the diagnostic problems and the princi routine management It is essential for the patient to visit periodically—at least once ever months—a physician specially experienced in the of diabetes mellitus The need for such surveillance emphasised by the importance which insurance com attach to regular medical supervision of diabetic p

Should the initial treatment be in hospital, in a unit, or at home? Two features are essential in treatment (1) the patient must be adequately on diet, urine testing, insulin therapy, and matters, and (2) he should be emphatically told with reasonable care a normal life is attainable For reasons admission to hospital has many und features The routine of hospital life is far remov normality, and mere admission to hospital makes patient feel an invalid Similarly treatment at makes concentrated instruction difficult The with uncomplicated diabetes should be admitted hospital annexe or special convalescent home or so that with the minimum of medical supervision lead a more normal life than is possible in hospital should be able to select his diet from a buffet and instruction, and witness practical demonstrations aspects of routine therapy Such centres could only for initiating therapy, but for routine checks idea is not new, and would have been put into Leeds but for the war The Joslin group are such a scheme at Boston It should save money, the overheads of a hostel would be very than those of a hospital Hospital admission sh reserved for the complicated cases and not utilised routine stabilisation

Conclusion

The most important problem is the development of so called complications, and the evidence suggests the frequency and severity of these depend on duration of the disease and the degree of control essential, therefore, that we should diagnose the earliest possible moment and, once the di made, adopt all means to ensure adequate Sustained adherence to a diet is essential, the given to diet and insulin therapy seems to be the important single factor in good control Adherence diet does not imply starvation No sound yet been forthcoming to refute the contention of (1923) that the most important factor gov sulin requirement with any ordinary plan of diet is ot the carbohydrate content but the total calorie ontent The fact that at least ten years are necessary o assess the effect of a diet on the incidence of complica ions, and that at least 25% of the population have either the inclination to follow a diet nor the intelligence o comprehend what dietary control means should not ause despair The treatment of every diabetic patient an individual affair, and calls for an understanding ot only of diabetes mellitus but of many personal and ocial factors as well as for patience thoroughness in raining and continuity of supervision Finally, good ontrol necessitates attention to the blood sugar level nd the avoidance of hyperglycæmia. The criteria of ood control should be that the patient feels well and is apable of physical activity commensurate with age, that is weight remains steady and is within 10 lb of the ormal for age and height that both ketosis and hypo ycæmia are absent and that the blood-sugar level is ept as near to normal as possible

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ANTIBIOTICS IN CHRONIC BRONCHITIS

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BACTERIA are often distributed unevenly in the sputum in chronic bronchitis, with the result that single cultures of sputum specimens may fail to reveal all the bacterial species present (May 1952 1953) Cultures should be made from at least five different parts of each specimen or a single culture may be made from liquefied sputum (Rawlins 1953) Using these methods of culture, analysis of the association between pus in the sputum and organisms known to be potential pulmonary patho gens has shown that these organisms especially *Hæmophilus influenzæ* and the pneumococcus, are likely to be pathogens in chronic bronchitis (May 1953) Further evidence for this can be obtained by eradicating the presumed pathogens from the sputum by chemotherapy and noting any coincident improvement in the patient's condition This is the subject of the present report, which includes also some observations on the clinical value of chemotherapy in chronic bronchitis.

Materials and Methods

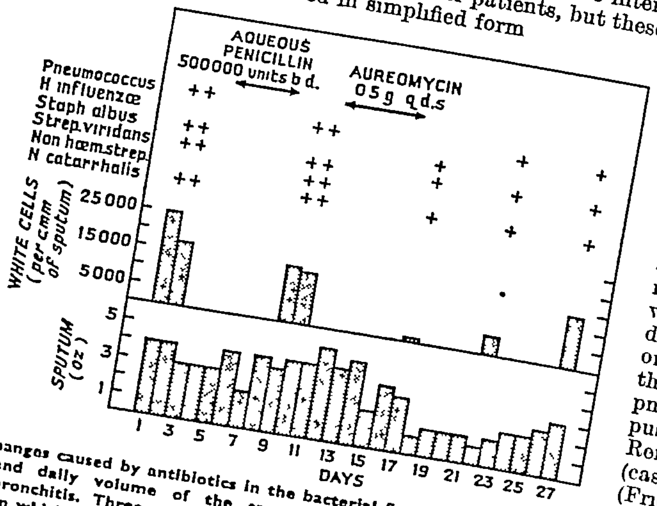
Patients investigated—All the patients investigated were attending the Brompton Hospital There were 18 inpatients, all of whom were expectorating either purulent or mucopurulent sputum and 21 outpatients The sputum of 4 outpatients was either purulent or mucopurulent and that of 17 was persistently mucoid during the period of observation

Collection of sputum—A specimen " of sputum is defined as a portion of sputum produced as a result of one bout of coughing only Specimens for bacteriological examination were expectorated into sterile universal " containers Cultures were made usually within three hours of expectoration of the specimen—never more than six hours. Owing to the variation of flora from one specimen to another (May 1953) at least 6 specimens were examined from each inpatient before and after chemotherapy It was not practicable to obtain more than 3 fresh specimens from outpatients. An interval of two days elapsed in every case between the end of chemotherapy and the examination of further specimens of sputum

Bacteriological techniques—Each specimen was rinsed in about five times its volume of sterile physiological saline solution to remove most of the adherent saliva Cultures were made on blood-agar by either the ' five culture method (May 1953) or a single culture after liquefaction of the sputum by pancreatin (Rawlins 1953) Cultures were incubated aerobically at 37°C for twenty four hours, after which appropriate diagnostic tests were made to identify the organisms isolated

Assessment of changes in patient's condition—Subjective changes in each patient's condition were noted but owing to the difficulty in assessing them, attention was paid mainly to changes in the pus content and to the daily volume of the sputum both of which can be measured with reasonable accuracy In the earlier investigations the proportion of pus was assessed by naked-eye inspection and by examination of stained films of the sputum Subsequently following the demonstration by G A. Rawlins (personal communication) that the cells in sputum were not destroyed by the pancreatin the pus cells were enumerated by a simple counting technique after liquefaction of the sputum The relative numbers of neutrophil and eosinophil polymorphs were determined by differential counts on stained films made from the liquefied sputum White-cell counts were made from time to time in many patients, especially those receiving chloramphenicol ume less ells, and derable When later the pus and the daily creased once more, H *influenzæ* had reappeared in the sputum Though the pneumococcus did not recur, and its exact relationship to the pus could not be assessed, probably this organism and H *influenzæ* were pathogens in this patient

This case has been described in detail to illustrate the use of antibiotics in assessing the significance of organisms in the sputum Similar reasoning was used in the interpretation of changes observed in other patients, but these findings will be presented in simplified form



Changes caused by antibiotics in the bacterial flora pus-cell content and daily volume of the sputum of a patient with chronic bronchitis. Three specimens of sputum were examined for each day on which cultures and counts of pus cells were made. The culture results shown in the chart were compiled by combining the observations made on the three specimens for each day, and the cell counts are the means of the results for each group of three specimens. The lume measurements show the total amount of sputum expectorated each 24-hour period.

E OF POTENTIALLY PATHOGENIC BACTE
ULENT SPUTUM (22 PATIENTS)

H *influenzæ*	*Staph aureus*	Hæmolytic streptococcus	Fried Länder bacill
–	–	–	–
–	–	–	–
–	+	–	–
+	–	–	–
+	–	–	
+	–	–	
+	–	–	

TH PURULENT SPUTUM

l 22 patients, all of whom ulent or mucopurulent any clinical evidence of o rise of temperature, and for the incapacity caused organisms isolated from may be considered most

be capable of causing potential pathogens—p *aureus*, group A r's bacillus. These wil

athogenicity as regards *idans*, non hæmolytic *atarrhalis*, and *Staph.* non pathogens."

motherapy was planned in each case to the "pathogens" one by one, but, as explained, this was not always practicable the "non-pathogens" were also noted, but in could the disappearance or reappearance of any organisms be correlated with the presence or pus in the sputum This fact suggests that these were truly non-pathogens

The incidence of "pathogens" in this series is in table I The pneumococcus and H *influenzæ* commonest, hæmolytic streptococci were not The effects produced by eradication of these by chemotherapy were as follows

Pneumococcus

Pneumococci were isolated from the sputum of patients (table I, cases 1–16) They were chemotherapy without interference with the flora in 14 instances In 5 of these the pn was the only "pathogen" In 1 (case 5) th disappeared completely after chemotherapy In 4 (cases 1–4) disappearance of the pneumococ accompanied by disappearance of pus and by in the volume of sputum Pneumococci were with *Staph aureus* in 3 patients (cases 6–8) disappeared from the sputum of 1 (case 6) when organisms were eliminated simultaneously In the 2 other patients (cases 7 and 8) removal of pneumococci was accompanied by disappearance pus, although *Staph aureus* remained in each Removal of pneumococci from the sputum of 7 (cases 9–15) from whom H *influenzæ* was also is (Friedländer's bacillus as well in case 9) led to reduction of the pus in 5 cases and no change in 2 quent removal of H *influenzæ* was accompanied appearance of the pus Simultaneous removal of cocci and H *influenzæ* from 1 patient (case 16) with a reduction in the amount of pus Rel which the reappearance of pus was also reappearance of pneumococci in the sputum observed in 3 patients In 7 others, whose relapse also observed, the "pathogen" was H *influenzæ* lapses were observed in which one or other of these ganisms was not found in the sputum

influenzæ

This organism was found in 14 patients (table I ses 9–22) It was removed from the sputum of 12 ases 10–15 and 17–22) without interference with the maining flora (6 of the patients in whom both *influenzæ* and pneumococci were present were treated st with penicillin to remove the pneumococci the rt played by *H influenzæ* as regards the pus that mained could then be assessed) In each instance the s either disappeared or was very much reduced. In 1 her patient (case 10) *H influenzæ* and a pneumococcus ere eliminated simultaneously with reduction in the nount of pus, whereas in 1 other (case 9) *H influenzæ* d Friedländer s bacillus were eliminated simultaneously, so with coincident disappearance of the pus The ily volume of sputum was reduced in each case when *influenzæ* was eliminated, but in no instance did utum disappear completely Relapses were observed in patients The time of relapse varied from three to elve days after the end of therapy, and in each instance *influenzæ* had reappeared in the sputum In 2 patients e reappearance of the pus preceded the finding of *influenzæ* by two or three days

taph aureus

Staph aureus was found in the sputum of only 3 atients (cases 6–8) and in each instance pneumococci ere also present Eradication of *Staph aureus* and neumococci simultaneously from the sputum of 1 atient was accompanied by disappearance of the pus n the 2 remaining patients the pus disappeared when the neumococci were removed, even though *Staph. aureus* as still present in the sputum

riedländer s Bacillus

Only 1 patient (case 9) was found to be harbouring riedländer s bacilli in his sputum but pneumococci and *influenzæ* were also present. The Friedländer s bacillus uld not be removed from the sputum independently of *influenzæ* and its importance in relation to pus in this atient could not be assessed

PATIENTS WITH MUCOID SPUTUM

Antibiotics were administered to 17 patients who were pectorating only mucoid sputum The patients may be nsidered in 2 groups

(1) Those in whose sputum no ' pathogens could be monstrated (11 patients)

(2) Those whose sputum contained pathogens" (6 tients: 3 with *H influenzæ* 2 with pneumococci and 1 th *Staph aureus*)

Since these were outpatients it was necessary to use antibiotic which could be taken by mouth Chlor phenicol was selected and given in 0 5 g doses three mes a day for five days. The daily volume of the sputum as measured by each patient for three weeks chemo erapy being instituted after the end of the first week ecimens of sputum were examined bacteriologically mediately before, 2 days after and 9 days after emotherapy

In no instance did chloramphenicol cause any alteration the daily volume of the sputum The flora of the utum of patients with no ' pathogens was always e same two days after therapy as it was before In ch of the 6 patients in whom pathogens were found ese organisms were eradicated by chloramphenicol and d not reappear in the following week. Organisms of the sumably non pathogenic group however were still sent in the sputum after therapy So the removal of athogens from patients producing purely mucoid utum apparently does not affect the amount expec rated.

EFFICIENCY OF ANTIBIOTICS

Penicillin was considered to be the antibiotic of choice for the treatment of pneumococcal infections. It was used for this purpose in each of 12 inpatients but not for outpatients, owing to the difficulty of giving regular injections Both aqueous sodium penicillin G and procaine penicillin were used Aqueous penicillin was given in doses of 500,000 units twice daily for five days to 5 patients and for seven days to 3 patients. One patient received 300 000 units of procaine penicillin twice daily for five days, and 3 patients received 600 000 units twice daily for five days. In every case the pneumococci were eradicated from the sputum and there was no need to have recourse to penicillin esters.

The number of relapses of pneumococcal infections after penicillin therapy was difficult to assess, since in many cases *H influenzæ* was also present, necessitating further chemotherapy which may have prevented pneumococcal reinfection Only 3 patients who received penicillin alone could be followed until relapse occurred In 1 the interval was eleven weeks in the 2nd three weeks and in the 3rd two days The sputum remained mucoid in each instance between the end of therapy and the reappearance of pneumococci in the sputum

Streptomycin 1 g twice daily was administered for five days to 5 patients with *H influenzæ* infections. *H influenzæ* was still present in the sputum of 1 patient at the end of the period of treatment It was absent from the other 4 patients sputa. Relapses, in which the reappearance of pus coincided with the reappearance of *H influenzæ* occurred in ten weeks, five days, five days and three days.

Aureomycin 0 5 g every six hours was given for five days to 4 patients with *H influenzæ* infections Neither *H influenzæ* nor the pus disappeared in 3 cases whereas in the 4th patient both *H influenzæ* and pus were removed temporarily The pus reappeared after six days, but *H influenzæ* could not be found in the sputum until two days later One patient who received aureomycin for fourteen days remained free from *H influenzæ* and pus for four weeks.

Chloramphenicol was used more than other antibiotics in the treatment of *H influenzæ* infections because it seemed to be the most efficient agent for the removal of this organism The rapidity with which relapses occurred, however was disappointing and it is doubtful whether the results justify the routine use of this antibiotic in view of the possibility of blood dyscrasias being produced The results obtained with chloramphenicol are shown in table II.

OTHER EFFECTS OF ANTIBIOTICS

In every patient with a purulent sputum in this series some form of chemotherapy eliminated or greatly reduced the pus and usually diminished the quantity of sputum expectorated. Such changes were not necessarily accompanied by subjective improvement in the patients

TABLE II—EFFECT OF CHLORAMPHENICOL ON INFECTIONS ASSOCIATED WITH *H influenzæ*

Case no	Dosage of chloramphenicol (g)		Sputum after therapy		Time of relapse (days)
			H influenzæ	Pus	
10	0 5 q d.s.	5 days	Absent	Absent	3
12	,,	,,		,,	3
17	,, ,,			,,	8
21	,, t.d.s.	,,		,,	5
22	,, q d.s.	7 days	,,	Less	[illegible]
11		11 days	,,	Absent	5
9	,, t.d.s.	12 days		,,	10
13	,, q d.s.	14 days	,,	,,	12
14	,, ,,	,,	,,	,,	9
15	,, ,,		,,		[illegible]
18	,, ,,	,,	,,	,,	5

condition In only 1 patient (table I, case 5) was the expectoration of sputum completely suppressed This patient felt very much better All the other patients, however, were left with a mucoid sputum after chemotherapy, and in many instances this sputum was extremely tenacious and difficult to expectorate These patients complained of increased dyspnœa and were troubled by their unproductive cough In such cases the reappearance of pus and an increase in the volume of sputum was often accompanied by subjective improvement, apparently associated with the loosening of bronchial secretions Unfortunately no means were apparent whereby it could be predicted before therapy which patients were likely to respond in this way

The rapidity with which the sputum returned to its former state after chemotherapy has already been described In 6 patients the reappearance of pus in the sputum was associated with clinical evidence of acute bronchitis In 5 cases three or more antibiotics had previously been administered, the 6th patient had received only one antibiotic

Discussion

In an earlier communication (May 1953) the organisms known to be able to cause acute pulmonary infections (potential pathogens) were shown to occur significantly more often in purulent than in mucoid sputa in chronic bronchitis This suggested that one or more members of the group could cause infections in this condition as well as in acute pulmonary disease The present investigations were undertaken to test this hypothesis further, and the results are in complete accord with the earlier findings Two organisms, *H influenzæ* and the pneumococcus, seem to be far more important than any others in chronic bronchitis

It may be argued that the therapeutic test has only a limited value in this type of disease There is always the possibility that an antibiotic may have effects other than the elimination of recognisable bacteria, and that improvements observed in the patient's condition do not necessarily result from removal of these organisms This, of course, is true, but the repeated observation of the disappearance of pus when *H influenzæ* and pneumococci are eradicated from the sputum, together with the reappearance of pus when they return, makes the probability of cause and effect a strong one The number of patients studied was small, but the results seem likely to be significant since they confirm the observations of Mulder et al (1952) and Stuart Harris et al (1953), who reported on the importance in chronic bronchitis of *H influenzæ* and the pneumococcus respectively

The part played by bacterial infection in the pathogenesis of the clinical state customarily referred to as chronic bronchitis has not been assessed in these investigations In most patients chemotherapy seems able only to render a purulent sputum mucoid, and patients with mucoid sputum apparently do not benefit from antibacterial treatment This suggests that, in established chronic bronchitis, bacterial infection is a secondary phenomenon Its importance as a cause of the hypersecretion of mucus, which is apparently of fundamental importance in chronic bronchitis (Oswald et al 1953, Reid), has not been assessed, nor has any attempt been made to define the rôle of viruses Stuart-Harris et al (1953), who investigated the association between influenza virus infection and bronchitis, found that this association was most frequent during acute exacerbations These have not been studied in detail in the present investigations

The organisms of doubtful pathogenicity in the lungs, especially *Strep viridans*, non-hæmolytic streptococci, and *N catarrhalis*, are found almost universally in both purulent and mucoid sputa The fact that their incidence is the same in the sputa and throats of the same patients (May 1953) suggests that they represent simply a extension of the flora of the upper respiratory tract a bronchial tree sufficiently damaged to be unable dispose of them efficiently It is possible, of course, these organisms are really only contaminants from mouth and are added to the sputum as it is expector This is unlikely, however, since in this investigation was found that they were still present in large in pieces of mucoid sputum which had been very washed to remove any adherent saliva

The evidence, then, from bacteriological and therapeutic studies suggests that in chronic the mucus in the affected parts of the bronchial colonised more or less evenly by organisms from upper respiratory tract, most of which are non If infection takes place, as manifested by the pro of pus, it is usually caused by *H influenzæ* or by pneumococcus These organisms are often distributed in the sputum, and possibly this irre reflects a patchy distribution of infection in the chial tree The histological observations of confirm the hypothesis that the infected areas irregularly scattered throughout the lungs and not necessarily coincide with the sites of mucus

Though these investigations were not planned to assess the place of antibiotics in the treatment chronic bronchitis, certain observations have been which seem to bear directly on this matter (1) patients feel worse rather than better after chemoth owing to the difficulty in expectorating their tenacious mucoid sputum, and (2) the rel especially of *H influenzæ* infections, is high, and in cases the reappearance of pus in the sputum is panied by fever and malaise Though many undoubtedly feel much better for some time after therapy, these disadvantages should strike a n caution about the indiscriminate use of anti chronic bronchitis

Summary

The significance of organisms in relation to pus sputum in chronic bronchitis has been inv by determining the changes in the sputum brought by antibiotics

Two organisms, *Hæmophilus influenzæ* and pneumococcus, seem to be far more important than others in chronic bronchitis

Purulent sputum can be rendered mucoid and diminished in quantity by suitable chemotherapy in most patients relapses, especially of *H* in infections, occur rapidly after the discon treatment These relapses may be accompanied by and malaise

Patients expectorating only mucoid sputum do seem to benefit by chemotherapy, no matter bacteria are present

The change from purulent to mucoid sputum b about by chemotherapy makes some patients feel than they did before therapy This is due to the viscidity of their mucoid secretions, which are h to expectorate and cause increased dyspnœa

I wish to thank Dr Neville Oswald for his unfailing agement and coöperation and for permission to inve his patients, and Mr G A Rawlins for his invaluable tec assistance

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SPUTUM IN CHRONIC BRONCHITIS

EFFECTS OF ANTIBIOTICS

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THE seriousness of the effects of chronic bronchitis, pecially in middle aged and elderly men in our large ndustrial towns, is emphasised by Goodman et al 1953) Chronic bronchitis causes not only many deaths ut also a serious loss of working time

Although many of the patients remain relatively well luring the summer they cannot obtain continuous mployment because they become much more seriously lisabled when autumn arrives In autumn and winter heir sputum becomes more profuse and purulent and heir dyspnœa increases. The cause of these acute xacerbations is little understood. Stuart Harris et al 1953) found no significant difference between the acterial flora of the sputum in exacerbation and that n "relative quiescence but they do not state whether oth groups had purulent sputum or whether the uiescent cases had only mucoid sputum It would be urprising if the development of purulent from mucoid putum were not associated with at least a quantitative hange in the bacterial flora Stuart Harris et al also ound that the bacterial flora closely resembled that ound in the upper respiratory tract of healthy people, nd conclude that 'in chronic bronchitics there is essen lally a failure of defence of the lower respiratory tract gainst invasion by nasopharyngeal organisms,' which hey attribute to preceding infections

The autumn exacerbations are probably due to further amage to the epithelium of the lower respiratory tract y virus infections or by atmospheric irritants which reate conditions favouring proliferation of organisms om the upper respiratory tract Little can be done to revent these predisposing injuries but if the subse uent bacterial proliferation were controlled by anti otics, the severity and duration of the acute exacerba ons might be reduced. To achieve this it would be cessary either to administer the antibiotic continuously roughout the winter or to start giving it at the first mptom of each exacerbation Either of these methods at especially the former would carry the risk of acquired cterial resistance to antibiotics.

A preliminary study of the changes in the bacterial ora of chronic bronchitic sputum produced by various antibiotics and the development of resistance was made on a small group of bronchitics who received courses of penicillin chloramphenicol aureomycin and sulphadimidine

MATERIAL

Since many specimens of sputum were required, 13 patients with chronic bronchitis were selected from the outpatients of Hammersmith Hospital who because of the severity of their bronchitis were unemployed and could attend daily without financial loss. They attended a weekly clinic and brought specimens of sputum to the bacteriological department on intervening days At the clinic the severity of their exertion dyspnœa was estimated according to five grades of severity (Fletcher 1952) A note was made of subjective changes in dyspnœa cough, and sputum Details of the patients are given in table I

Courses of Treatment

The 13 patients received between them twenty four courses of treatment between October 1952 and March 1953 (table I)

Penicillin was given orally in seven-day courses during which 200 000 units was given four hourly during the day (five doses) making 1 000 000 units in each twenty four hours Three of the courses were given without any antibiotic therapy having been given in the preceding three months Courses were also given to 3 patients who had each had a course of chloramphenicol six weeks previously (2 of these had each had also a course of penicillin six weeks before the chloramphenicol) and to 2 patients who had had a course of aureomycin six weeks previously In these cases the bacterial flora appeared to have regained its pretreatment status before the penicillin was given. Oral penicillin was used because we considered that parenteral administration would be impracticable for prophylactic purposes. We feared that larger doses would give rise to severe gastro intestinal disturbances In 3 cases we found a serum penicillin level higher than 1 unit per ml two hours after the last dose

Chloramphenicol was given in seven-day courses of 500 mg four times daily to 4 patients 2 of these had had oral penicillin six weeks previously and their bacterial flora had regained its pre treatment status

Aureomycin was given in seven-day courses of 500 mg four times daily to 5 patients, of whom 2 had a second five-day course of the same dose 5-9 weeks later when their bacterial flora had regained its previous status.

Sulphadimidine was given in seven-day courses of 1 g four times daily to 4 patients who had had no preceding treatment

Methods

Bacteriological

Specimens of sputum coughed up during the first two hours after waking were examined twice before treatment, daily during treatment, on alternate days during the next week, and thereafter at longer intervals.

TABLE I—DETAILS OF CASES

Case	Age (yr)	Sex	Grade of dyspnœa	Amount of sputum	Length of history of bronchitis (yr)	Courses of treatment		
						1st	2nd	3rd
1	66	M	4	+ +	35	Aureomycin 7 days	Aureomycin 5 days	Penicillin
2	61	M	4	+ +	20	Aureomycin 7 days	Aureomycin 5 days	Penicillin
3	66	M	3	+	15	Penicillin	Chloramphenicol	Penicillin
4	68	M	3	+	12	Penicillin	Chloramphenicol	Penicillin
5	60	M	3	+	7	Chloramphenicol	Penicillin	
6	53	M	4	+	14	Chloramphenicol	Penicillin	
7	63	M	4	+ +	30	Sulphadimidine	Aureomycin	
8	42	F	3	+	8	Aureomycin 7 days		
9	63	M	4	+ +	00	Aureomycin 7 days		
10	56	M	4	+	25	Sulphadimidine		
11	46	M	3	+ +	6	Sulphadimidine		
12	63	M	4	+ +	4	Sulphadimidine		
13	68	M	3	+	35	Penicillin		

The method of examination was as follows

5 ml of sputum was washed in a saturated solution of sodium chloride to minimise salivary contamination, and next added to 5 ml of physiological saline solution and homogenised by mechanical shaking for an hour at 37°C in bottles containing glass beads This homogenisation was done in view of the heterogeneous distribution of organisms in sputum (May 1952) Duplicated samples of 30 sputa homogenised by this method were found to contain the same organisms in the same relative proportions

From this suspension viable counts by Mitchison's (1953) method, cultures on blood agar medium, and "gutter plate" sensitivity tests were set up with a standard loop The plates used for sulphonamide sensitivity tests contained 5% laked horse blood The gutters contained penicillin 10 units per ml, aureomycin 25 µg per ml, chloramphenicol 50 µg per ml, and sulphadimidine 10 mg per ml A test on a control sensitive organism (*Neisseria catarrhalis* for sulphadimidine, *Staphylococcus aureus* for the remaining antibiotics) was included on each plate Further aureomycin sensitivity tests were made by inoculating colonies on to agar plates containing 1, 2, 4, 6, 8, and 10 µg per ml

The plates were examined after eighteen hours' incubation at 37°C The organisms were identified and their total number, relative proportions, and antibiotic sensitivity recorded

Microscopic

Two smears of each specimen were examined They were made from the thickest area of sputum before it was washed, were fixed wet in Carnoy's fluid for a minute, and stained with pyronine methyl-green (Brachet 1942) and 0 5% toluidine blue in pH 4 5 buffer Both were stained for twelve hours, dehydrated quickly in two changes of tertiary butanol, and mounted in D P X These preparations were especially suitable for examination in polarised light to show up the extracellular structure of the sputum, and were analysed in a similar manner to that described by Elmes and White (1953) Viscidity was not measured

The following characteristics of each specimen were recorded total cellularity, profusion of polymorphs, mononuclear inflammatory cells, epithelial squames, clumps of bacteria, dust cells, and Curshman's spir and density of mucoprotein fibre network and deoxyribonucleoprotein fibres

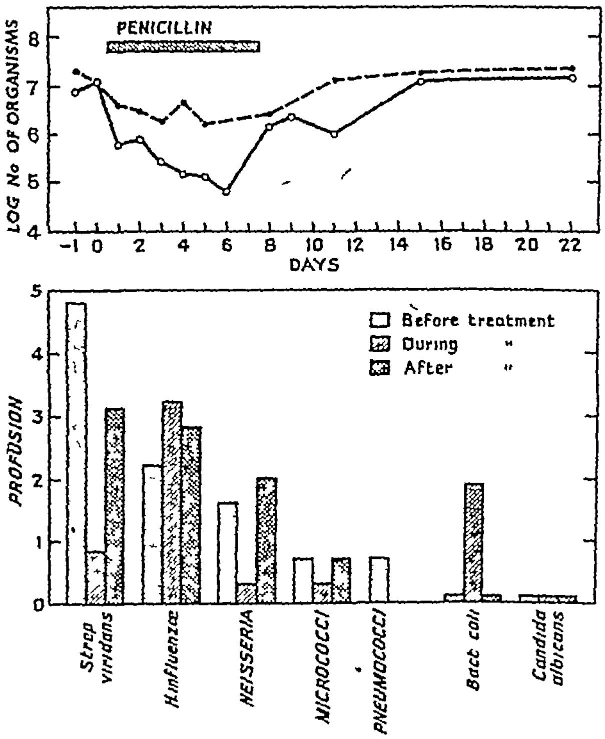

Fig 1—Average effect of penicillin on total bacterial count (above) and on relative profusion of individual organisms (below) open circles first course solid circles second course

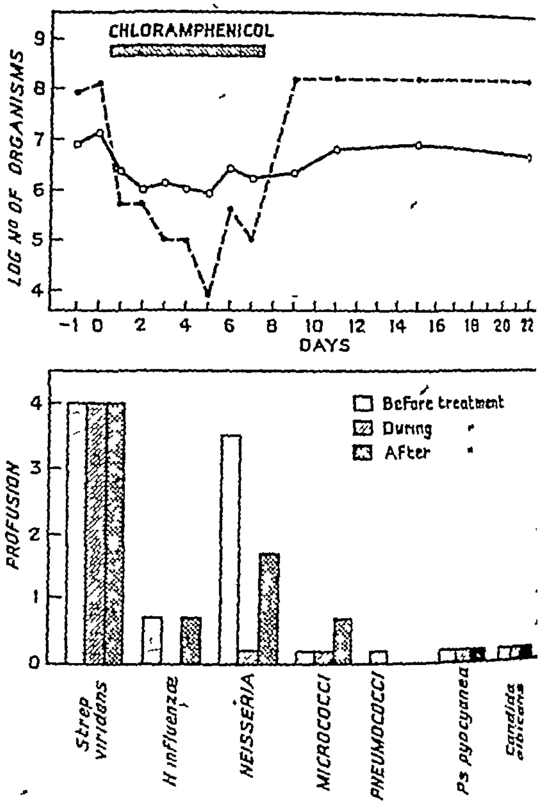

Fig 2—Average effect of chloramphenicol on total bacterial co (above) and on relative profusion of individual organisms (bel open circles, average of 3 patients, solid circles, case 4.

Areas in the smears showing bacterial clumps and epithelial squames were taken to originate from sal and were ignored in the cellular and fibre estimat The mucoprotein was distinguished from the deox ribonucleoprotein in the films stained with pyron methyl green by the sign of birefringence with a ¼ compensator The mucoprotein showed positive a birefringence, and the nucleoprotein fibres negativ axial birefringence

Results

Flora

In the pre treatment specimens *Streptococcus virid* was most frequently the predominant organism (11 of 13 patients) *Neisseria pharyngis* was present in patients, and *Hæmophilus influenzæ* in 8 Micro were present in 8 patients but only in scanty num *Strep pneumoniæ* was isolated from 2 patients, be predominant in 1 of these *Candida albicans* was iso from 4 patients, but in each it formed only a proportion of the whole flora

During treatment a decrease in the total numb viable organisms and an alteration in the proport of different organisms in the flora were noted.

To illustrate our findings we have combined the of all courses of treatment by each drug This see justified since all the responses were closely sim except that which followed one course of chlor phenicol This is illustrated separately The total co are expressed as the average logarithm of the of organisms per ml The changes during treatment shown graphically in figs 1–4 The relative pr of the organisms are expressed as the average of arbi values (profuse growth = 5, moderate growth = scanty growth = 1) This average value of each or fore during, and after treatment is shown by stograms

ffect of Penicillin

Fig 1 shows the effect of penicillin in the nine courses treatment The total number of organisms was duced but returned to the pre treatment level a week ter treatment A second course of treatment given 2 patients three months later produced a similar but ss pronounced effect The relative proportion of the ganisms was altered during treatment Among the nicillin sensitive organisms *Strep pneumoniæ* present 1 patient, disappeared completely *Strep viridans* as greatly reduced in number and there were fewer eisseriæ and micrococci No acquired resistance to enicillin was found Among the penicillin resistant rganisms *H influenzæ* initially present in 7 patients ecame the predominant organism in all except 1 *acterium coli* appeared for the first time in 6 patients nd *Pseudomonas pyocyanea* in 1 The number of *albicans* present in 1 patient, was unaffected

After treatment *H influenzæ* remained the predominant rganism for at least three or four weeks *Ps pyocyanea* emained present in small numbers and *Bact coli* isappeared within fourteen days. The penicillin sensitive rganisms returned to their pre treatment state within ourteen days

ffect of Chloramphenicol

Fig 2 shows the average effect of chloramphenicol iven to 4 patients The reduction in the total count was light in 3 patients but pronounced in the remaining atient owing to the disappearance of *H influenzæ* hich had been profuse The neisseriæ were reduced, nd the *Strep pneumoniæ* present in 1 patient dis ppeared. The remaining organisms were unaffected. fter treatment *H influenzæ* returned in profusion two ays after the cessation of treatment No acquired resistance to chloramphenicol was noted

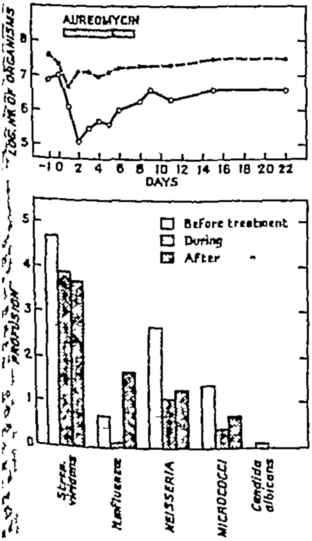

Fig 3—Average effect of aureomycin on total bacterial count (above) and on relative profusion of individual organisms (below): open circles first course; solid circles second course

Effect of Aureomycin

Fig 3 shows the effect of aureomycin in seven courses of treatment The reduction in the total count was considerable in the patients receiving the drug for the first time owing to a decrease in the number of all the organisms A second course of treatment given to 2 patients one and two months later had a similar but less pronounced effect

In all the patients the minimal inhibitory concentration of aureomycin for strains of *Strep viridans* isolated before treatment was 2 or 4 µg per ml that for strains isolated three days after the start of treatment was 6 µg per ml; and that for strains isolated four days later was 10 µg per ml Resistance remained after two months and was slightly increased when a second course of treatment was given *H influenzæ* and micrococci showed no acquired resistance The strains of *Strep viridans* from all the patients had become sensitive again two months after the second course of treatment

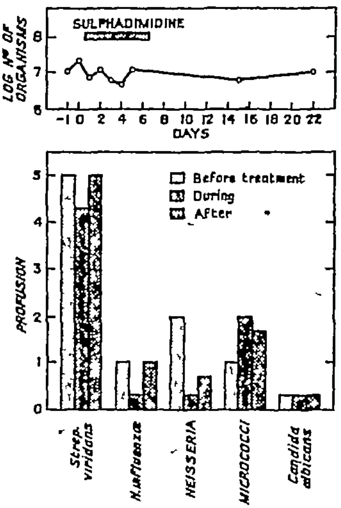

Fig 4—Average effect of sulphadimidine on total bacterial count (above) and on relative profusion of organisms (below)

Effect of Sulphadimidine

Fig 4 shows the average effect of sulphadimidine given to 4 patients. The reduction in the total count was slight in all the patients and was due to a reduction in the numbers of *Strep viridans H influenzæ* and the neisseriæ

Microscopy

In all the patients polymorphs were present in considerable numbers before treatment was started, although in some the sputum was macroscopically mucoid. This probably indicates persistent active inflammation of some part of the bronchial tract During exacerbations of symptoms there was a tendency for polymorphs and fibrous nucleoprotein to increase and for the sputum to become purulent Thus our findings confirm those of Elmes and White (1953) That this should happen with the appearance of a pneumococcus or *H influenzæ* is not surprising but it also happened in exacerbations which seemed to be due to ' colds or to fog without the emergence of any generally recognised pathogen in the flora of the sputum

To study these causes of bronchial inflammation more quantitatively the sputa were classified according to the microscopical findings into purulent and non purulent specimens. In table II the frequency of the two types in all the specimens is related to the presence of moderate or profuse growth of *Strep pneumoniæ* and *H influenzæ* and to the incidence of fog during the preceding three days It will be seen that there is a significant association between purulent sputum and significant growth of *H influenzæ* Only 2 patients had *Strep pneumoniæ* hence there were too few specimens to show any association with purulence The association with fog was suggestive but not significant. In the absence of any of these influences the sputum was significantly less often purulent

TABLE III—EFFECT OF FOG ON SPUTUM

H influenzæ	Fog	No of sputa showing purulence graded as					Total	P
		—	±	+	++	+++		
Absent	Present	5 (6 7%)	30 (40%)	19 (25 4%)	18 (24%)	3 (4%)	75	0 7–0 5
	Absent	9 (6 5%)	63 (43 4%)	47 (32 4%)	21 (14 5%)	5 (3 4%)	145	
Present	Present	0	6 (11 8%)	11 (21 6%)	23 (45%)	11 (21 6%)	51	0·02–0·01
	Absent	0	11 (12·2%)	36 (40%)	38 (42 2%)	5 (5 6%)	90	

P was determined by χ^2

To study further the effect of fog the cases were divided into those with and those without any growth of *H influenzæ* in foggy and non-foggy weather (table III) This showed that fog had a significant effect in increasing the purulence of the sputum only in patients with *H influenzæ* in their sputum

During periods of treatment it was found that, when the total bacterial count was reduced for more than three days, or when *Strep pneumoniæ* or *H influenzæ* disappeared, the sputum became mucoid and polymorphs were scanty Bacteriological relapse was followed by a return to the status quo ante When the treatment was bacteriologically ineffective, there was no change in the microscopical characteristics of the sputum

Clinical Results

Since our chief interest was in the effects of the drugs on the bacteriological flora of the sputum, the courses of treatment were guided by these findings rather than by clinical indications, except in 1 patient who had a severe exacerbation requiring admission to hospital, when he was treated successfully with oral penicillin

TABLE II—CLASSIFICATION OF SPUTA

Cause of inflammation	No of purulent sputa	No of non purulent sputa	P
*Strep pneumoniæ**	3	3	<0 001
*H influenzæ**	62	42	0 1–0 05
Fog	52	74	<0 001
Remainder	32	128	
Total	125	236	

* Present in moderate or profuse numbers

P was determined by χ^2, the distribution of each group being separately tested against the total remaining

With this exception the clinical effects of the courses of treatment were not striking In a third of the cases the courses appeared to give some relief of dyspnœa and cough, but this response was no more than might have been achieved by a placebo A properly controlled trial with objective assessment of pulmonary function would be necessary to show whether or not short courses of antibiotic treatment do any good in chronic bronchitis except during acute exacerbations

Aureomycin caused diarrhœa in four of the seven courses, chloromycetin in two out of four, and penicillin in one out of nine

Conclusions

Penicillin, in the dose that we used, was effective against most of the bacteria in the sputum, but it allowed, or even encouraged, the emergence of *H influenzæ* as a dominant organism, and this we found to be associated with increase in the purulence of the sputum, especially during foggy weather It would therefore be unwise to use penicillin for continuous prophylaxis throughout the winter, and it has been shown by Kuh and Collen (1949) that such administration has little effect on the incidence of respiratory infection in large groups of the general population Penicillin might be suitable for administration intermittently at the onset of any acute exacerbation It would probably be effective in the dose we used xacerbations due to *Strep pneumoniæ*, but to protect against exacerbations due to *H influenzæ* large parenteral doses perhaps combined with streptomycin (Mulder et al 1952) would be required, which would scarcely be practicable except on a very limited scale

Chloramphenicol had a surprisingly small effect on the general bacterial flora It was effective against *H influenzæ* and might be most useful, but the danger of agranulocytosis following its repeated or prolonged use renders it unsuitable for prophylaxis

Aureomycin was the most effective of the drugs against the whole bacterial flora but it produced resistance in *Strep viridans* and a second course, while resistant strains were still present, proved less effective than the first Thus it appears unsuitable for prophylactic use either continuously or intermittently

Sulphadimidine had very little effect on the general bacterial flora Continuous administration in small doses throughout the winter has no prophylactic effect against winter exacerbation of bronchitis in cases of pneumoconiosis (Kilpatrick 1953) Larger doses could hardly be used without risk of toxic effects Intermittent administration might well be of value against exacerbation due to *Strep pneumoniæ*, but, until we know the frequency with which this organism rather than *H influenzæ* and the other denizens of the sputum is responsible for the exacerbations, we cannot forecast how useful it would be

Our conclusion is that none of the drugs we used would be suitable for prophylaxis of acute exacerbations of chronic bronchitis The requirements of a drug for this purpose are that it should be cheap, free from toxic effects, effective against the whole range of bacteria responsible for chronic bronchitis, and not likely to impart acquired resistance If and when such a drug becomes available, an enormous amount of disability in men of working age might be prevented

Summary

A small group of patients with chronic bronchitis were given short courses of penicillin, aureomycin, chloramphenicol, and sulphadimidine

The bacteriological and microscopical changes in the sputum and the clinical effects were observed Although each drug, except sulphadimidine, temporarily reduced the bacterial counts and the purulence of the sputum, the clinical effects were slight

For various reasons none of the drugs appeared suitable for the prophylaxis of acute exacerbations.

Foggy weather appeared to have a more deleterious effect on cases with *H influenzæ* in the sputum

We are indebted to Prof Lord Stamp and Dr D Mitchison for advice and criticism

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ANAGEMENT OF ADRENAL CORTICAL FAILURE IN MENINGOCOCCAL SEPTICÆMIA

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ACUTE adrenal failure in meningococcal septicæmia s been treated successfully by Grace et al (1940) with racts of suprarenal cortex by Banks and McCartney 43) with 'Eucortone' by Nelson and Goldstein 51) with intramuscular cortisone by Newman 51) with intravenous cortisone in patients whose nditions had deteriorated in spite of treatment with ract of adrenal cortex; and by Magnus (1953) th intravenous eucortone and deoxycortone acetate ccessively

We report here two cases in which eucortone and rtisone were given concurrently, with recovery of both tients

Case-records

Case 1 —A healthy schoolboy aged 15 had prodromal laise and lassitude for twenty four hours, followed by ffness of his legs and back He was found lying on his bed ghtly confused and with a temperature of 100°F at 10 P.M 10.30 P.M. he was examined by the school doctor who found neralised muscular weakness a weak rapid pulse and a techial rash. Lumbar puncture produced clear cerebrospinal id (C.S.F) under normal pressure and containing no organ ms or cells. At midnight the boy was seen by one of us M. B.) he was then extremely prostrated with systolic od pressure 50 mm. Hg (diastolic unobtainable) conjunc al suffusion and subconjunctival hæmorrhage faucial ection a rapidly spreading petechial rash and muscle derness There were no signs of meningitis. Meningococcal ticæmia was diagnosed provisionally and the patient was en intramuscular penicillin 1 mega unit and intravenous phadimidine 3 g

On admission to hospital at 1 30 A.M. next day he was fused but able to drink. Tachypnœa and tachycardia re severe Despite a blood pressure of 65/40 mm Hg and weak pulse his skin was warm and flushed, and peripheral nosis was present producing a purple lividity of nail beds, , cheeks and ears. The petechial rash was mainly distri ted over the distal parts of the limbs with only scanty ions on the trunk.

Treatment —Eucortone 10 ml and cortisone 100 mg were en intramuscularly on admission. At 4 A M intravenous ortone 20 ml was given At 5 A.M. a 5% glucose saline usion of 20 oz. was started and intravenous sulphadimidine was given. At 6 A.M intravenous eucortone 20 ml was n and a plasma infusion was started. Though he was still scious, with pronounced hypotension the patient was lious and could no longer coöperate Oxygen therapy by sk was attempted. At 9 30 A.M restlessness and delirium re extreme and peripheral lividity was still present but blood pressure was unrecordable The restlessness and rosis decreased when the boy was put in an oxygen tent ger's solution was substituted for plasma. Intramuscular tisone 100 mg was given and a course of intravenous rtone 10 ml. two hourly was started At 1 P.M a slow sion of plasma was begun Intravenous sulphadimidine and intramuscular penicillin 500 000 units eight-hourly given At 10 P.M the pulse-rate was 130 and blood ssure 70/40 mm. Hg Glucose drinks were taken in small ntities.

Third Day.—At 4 A.M Ringer's solution was substituted for ma because the levels of serum and urinary chlorides were porarily below normal though the blood sugar level had ained normal At 9 A.M the pulse rate was 110 and blood ssure 75/15 mm. Hg The dose of intravenous eucortone changed to 10 ml four hourly At 4 P.M., since there was evidence of overloading of the circulation and mouth feeding was practicable intravenous infusions were stopped The total urinary volume since admission was 73 oz. The serum potassium level had fallen to 12 mg per 100 ml. (3 1 m.eq per litre) This deficiency was corrected by giving potassium chloride 2 g daily by mouth for three days Intramuscular eucortone 10 ml was now being given four hourly and the dosage of sulphadimidine was changed to 1 5 g eight hourly by mouth and of penicillin to 500 000 units b d At 10 P M the patient was comfortable with pulse-rate 100 and blood pressure 85/50 mm Hg A course of cortisone 25 mg by mouth was started

Fourth Day —Cortisone 12 5 mg was given by mouth every six hours, and intramuscular eucortone 10 ml four hourly Penicillin and sulphadimidine therapy was continued

Fifth Day —The patient began to take solid food and his blood pressure remained steady Eucortone therapy was discontinued

Further Progress —The dosage of cortisone was reduced to 25 mg on the seventh and eighth days, and to 12 5 mg on the succeeding four days The total oral dosage was 275 mg in eleven days. Throat, nose, and skin cultures, taken on the day after chemotherapy had been started were sterile Oliguria did not develop; proteinuria and reduced urinary secretion of chloride were transitory The only electrolyte disturbance was a temporary fall in the serum potassium and plasma-chloride levels on the third day the blood sugar level remained normal The patient was discharged fit after twenty eight days with a blood pressure of 125/65 mm Hg

TABLE I—FLUID BALANCE BLOOD UREA LEVELS, BLOOD PRESSURE, AND DOSAGES OF EUCORTONE AND CORTISONE IN FIRST SIX DAYS OF TREATMENT OF CASE 1

Days	2	3	4	5	6	7
Intake						
Water (oz.)	2	56	87	107	108	90
Plasma (oz.)	90	—	—	—	—	—
Ringer's solution (oz.)	10	35	—	—	—	—
5% Glucose saline solution (oz)	20	—	—	—	—	—
Total	123	91	87	107	108	90
Output						
Vomit (oz)	10	—	—	—	—	—
Urine (oz.)	43	63	58	60	79	105
Total	53	63	58	60	79	105
Blood urea (mg per 100 ml.)	105	59	—	—	—	62
Systolic blood pressure (*mm Hg*)						
Highest	90	84	100	90	95	105
Lowest	40	70	80	80	80	90
Eucortone (*ml.*)						
Intravenous	120	60	—	—	—	—
Intramuscular	10	20	60	30	—	—
Cortisone (*mg*):						
Intramuscular	200	—	—	—	—	—
Oral	—	25	50	50	50	25

Fluid balance, blood urea levels, blood pressure, and intake of eucortone and cortisone in the first week of treatment of case 1 are shown in table I

Case 2 —A cretin aged 45 who had been treated from the age of 3 years with thyroid extract complained of sudden feverishness, vomiting headache backache and, later in the day abdominal pain.

On admission to hospital at 10 P.M. on the second day of illness he was mentally alert pale cyanosed, and sweating with an extensive purpuric rash and neck rigidity

Investigations —Lumbar puncture produced turbid C.S.F under increased pressure and containing polymorphs and gram negative diplococci. The blood pressure was 130/70 mm. Hg

Treatment —Intravenous and oral sulphadiazine and intrathecal penicillin were given

Third Day —At 2 A.M the blood pressure fell suddenly to 85 mm Hg Intravenous eucortone 10 ml and intramuscular eucortone 10 ml. with intramuscular deoxycortone acetate 10 mg were given and an intravenous saline infusion was started. Intravenous eucortone 10 ml hourly was continued At 8.30 A M the blood pressure was 50/30 mm. Hg Intravenous eucortone 20 ml was given and a plasma drip was substituted for the saline infusion. Intravenous eucortone 10 ml. half hourly was continued until 2.30 P.M after which intramuscular eucortone 10 ml was given hourly with three additional intravenous doses of 10 ml. each At 10 A.M the blood pressure was 70 mm. Hg Cortisone therapy 25 mg. six hourly by mouth was started During the afternoon the intravenous infusion was stopped for fear of overloading the circulation

TABLE II—FLUID BALANCE, BLOOD UREA LEVELS, BLOOD PRESSURE, AND DOSAGES OF EUCORTONE AND CORTISONE IN FIRST SIX DAYS OF TREATMENT OF CASE 2

Days	2	3	4	5	6	7
Intake						
Borst diet (oz)	—	—	8	30	30	12
Milk (oz)	—	29	6	—	—	87
Water (oz)	2	70	—	—	—	—
Plasma (oz)	—	20	—	—	—	—
5 % Glucose saline solution (oz)	—	40	—	—	—	—
Saline solution (oz)	—	20	40	—	—	—
Total	2	179	54	30	30	99
Output						
Urine (oz)	4	13	Nil	8	28	54
Blood urea (mg per 100 ml)	—	86	160	162	—	147
Systolic blood-pressure (mm Hg)						
Highest	130	100	70	80	100	100
Lowest	—	40	40	60	60	60
Eucortone (*ml*)						
Intravenous	—	220	160	—	—	—
Intramuscular	—	80	80	150	60	60
Cortisone (mg) by mouth	—	100	150	100	37 5	50
Deoxycortone acetate (mg)	—	10	—	—	—	—

because no urine had been passed since the morning A catheter was passed, and only 1 oz of urine was obtained. Sulphadimidine was substituted for the sulphadiazine, and the patient was put into an oxygen tent

Fourth Day—Anuria was still present Intramuscular penicillin was substituted for the sulphadimidine, and Borst diet for anuria was started The blood pressure rose in the evening to 70 mm Hg Intravenous eucortone 10 ml hourly for sixteen hours was given, and the dosage of cortisone was increased to 12 5 mg four hourly

Fifth Day—The blood pressure rose gradually, and 8 oz of urine was passed The dosage of eucortone was changed to 10 ml four hourly intramuscularly until the ninth day, when the injections were given six-hourly until they were stopped on the eleventh day The dose of cortisone was gradually reduced from the fifth day and stopped on the twelfth day Deoxycortone acetate 10 mg was given on the eighth day and 5 mg on the tenth day

Further Progress—The plasma chloride, serum sodium, and blood sugar levels remained normal throughout the illness The serum potassium level fell to 14 mg per 100 ml (3 6 m.eq per litre) on the fifth day and to 13 mg per 100 ml (3 3 m eq per litre) on the seventh day This was corrected by adding potassium citrate and milk to the diet Progress was satisfactory after the eighth day except for a proteus infection of the urine, for which aureomycin was given The C S.F contained polymorphs, and the protein therein was increased and sugar reduced for twenty days in all The patient was discharged fit after forty five days, and his blood pressure was 120/65 mm Hg after thirty days

Fluid balance, blood-urea levels, blood-pressure, and intake of eucortone and cortisone in the first six days of treatment of case 2 are shown in table II

Discussion

Gross hæmorrhage starting in the adrenal medulla and spreading out into and disrupting the cortex has often been described in meningococcal septicæmia complicated by adrenal cortical failure. Morison (1943) suggested that this change was not the cause of the adrenal failure but was secondary to peripheral vascular failure initiated by the septicæmia Schwarz (1946) attributed the clinical state primarily to destruction of the medulla, but necropsy material examined by Banks and McCartney (1943) from one of their patients who died of meningococcal encephalitis showed extensive adrenal medullary hæmorrhage though the clinical picture of adrenal failure had not been present

The work of Rich (1944) in this respect deserves consideration He described a striking transformation of the solid cords of the zona glomerulosa into tubular structures containing fibrinous exudate, these changes in some circumstances were only associated with a few petechial hæmorrhages He considered this to be an initial pathological change which, sometimes in adults and usually in children, is obscured later by massive hæmorrhage Some of the appearances described by [illegible] McCartney (1943) seem to be similar

Although in the two present cases we lack histolog proof, we think that, if changes similar to those describ by Rich did take place, they were reversed by the ear use of antibiotics, coupled with massive replacement therapy

These two cases corresponded to the pure adrenal typ described by Banks and McCartney (1943) who emphasised the value of eucortone in treatment, considering th its use might be life saving, whereas in the encephali type the outcome was always fatal

We feel that certain clinical features are worth emphasising The combination of severe and prolonged hypotension with warm flushed cyanotic extremities and comparative mental and physical well being which evident in both of the present cases, except for a cri hour in case 1, contrasts with the cold pallor of extremities seen in hypotensive states due to conditions, and in our opinion is a most import diagnostic feature

The management is best discussed under two headings general and specific In the general management emphasise the importance of oxygen therapy in controlling anoxia, in particular the restlessness cerebral anoxia, and in this respect the oxygen seems to be superior to other methods, and was life saving in case 1 Control of the fluid balance is vital importance, and care is necessary to prevent overloading of the circulation The temptation to intravenous therapy in the presence of prolonged hypotension is strong but should be resisted unless dehy or electrolyte imbalance is present It is p undesirable when a substance which promotes the re tion of sodium—e g , cortisone—is used and when may be present This anuria seems to be unpred because, though both patients had severe hypotension, one secreted urine and the other did Some slight overloading of the circulation developed both cases For this reason we feel that long- substances—e g , deoxycortone acetate—should not used in this type of adrenal cortical failure

As regards biochemical disturbance, the serum and plasma chloride levels remained normal in both in contrast with the grave disturbance seen in crises Hypoglycæmia, mentioned by Nelson Goldstein (1951) and Banks and McCartney (1943), not develop, presumably because of the administration of cortisone and eucortone The urea level rose to 105 mg per 100 ml on the third in case 1, and to 165 mg per 100 ml on the fifth case 2, who developed anuria The serum pota level fell to 12 1 and 13 0 mg per 100 ml on the and fourth days respectively in case 1, and to 14 1 13 0 mg per 100 ml on the fifth and seventh respectively in case 2 This can also be attributed part to hormonal therapy, and was corrected by g potassium salts and milk by mouth

In considering the use of specific treatment eucortone and cortisone in these two cases we work the assumption that cortisone was slower than euco in action We therefore gave eucortone in very doses in the early stages, believing that such am were necessary to overcome the sudden rapid lo cortical function, and that in the past it had been in inadequate dosage

Since we did not know whether absorption from stomach in a desperately ill patient would be cortisone was given at first intramuscularly It has shown that an oral dose of 200 mg produces a blood level in an hour, and a maximal eo response, demonstrable for eight hours, after four (Nelson et al 1952) An intramuscular injecti effective in 6–8 hours

We therefore suggest that, in addition to the treatment of the infection, cortisone should be month in an initial dose of 100 mg followed by mg six hourly until the infection is controlled and patient is out of danger the dose being reduced to 5 mg six hourly for the following two days, and the al daily dose being thereafter halved every second y A large initial dose—e g 50 ml —of intravenous cortone should be given and followed by one of 20 ml hour later and further doses of 10 ml. hourly until systolic blood pressure is maintained at 80 mm Hg ese doses are large but the demands on the adrenal rtex are known to be great in the presence of severe ection.

Summary

Two cases of *meningococcal septicæmia and adrenal rtical failure, treated by eucortone and cortisone* are ported.

Both patients survived

During the critical stage of the illness, frequent large ses of eucortone intravenously and of cortisone by outh six hourly are advised in combination with tibiotics and oxygen therapy in a tent.

We wish to thank Dr A. M. Cooke for permission to publish e second case; Mr J R. P O Brien and Dr Paul Fourman r much valuable assistance and criticism; and the sister d nurses of Rowney ward for their unceasing care of the o patients.

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ICKLE-CELL TRAIT AND BLOOD-GROUPS IN GREECE

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THE sickle-cell trait has been known for many years to ccur sporadically in persons from Greece Choremis ervos, Constantinides, and Zannos (1951) first discovered local concentration of the trait in that country in nd around Petromagoula. Caminopetros (1952), using r very long periods the Scriver and Waugh (1930) tech ique of prolonged sealing up of blood without added agent, then claimed to have found a very high incidence mong Greeks in general, approaching 50% in Athenians. aminopetros s results could not be obtained regularly n the same blood.

The observations of one of us (Choremis 1952) had own that such frequencies certainly did not exist nd in our opinion (Lehmann 1953) the technique adopted was, in addition to showing genuine sickle cells almost certainly distorting normal red cells so that they some what resembled sickle cells In our view Caminopetros did not appreciate the fact that, as his results were obtained irregularly and could not be repeated every time on the same blood, only the chemical method could decide whether his claims were correct. In the Scriver Waugh technique bloods are tested by sealing up the specimen on a coverslip and incubating it. Under these conditions the leucocytes use up the oxygen in the confined space and eventually reduce the hæmoglobin. On prolonged incubation however changes may take place in the composition of the plasma which can exert external stresses on the red cells and alter the shape of normal red cells until they become remarkably like sickle cells (Isaacs 1950) The two types of sickle cells caused by external and by internal causes will be called in this paper "false" and "true" sickle cells respectively It was clearly desirable that a fresh survey should be made, using the much more rapid and reliable method of reducing hæmoglobin in the red cells by added reducing agents.

True and False Sickling

Pauling et al (1949) have shown that the sickle-cell trait, found characteristically in Negroes, depends on the presence in the red cell of a variable amount of an abnormal hæmoglobin with well defined physico-chemical properties which differentiate it clearly from normal hæmoglobin Reduced sickle-cell hæmoglobin has a very low solubility in water and in the red-cell fluid (Perutz et al 1951) Thus, on reduction the abnormal hæmoglobin will crystallise inside the red cells and the crystals will distort the cell envelope and give the cells the bizarre shape described as 'sickle cell' Some of the true sickle cells have two points only but there are always some and sometimes many with more than two points and with one or more sharp re-entrant angles. External stresses can, however distort the envelope of red cells containing only normal hæmoglobin to give them a shape resembling that of sickle cells. Under these conditions the cells are usually fusiform rather than sickle shaped they tend to retain something of a central bulge with drawn-out processes at each side. They seldom have more than two such points and if any re-entrants or embayments are present, they are rounded and not angular True sickle cells are arranged irregularly, but in 'sickling' due to external stresses the cells tend to arrange themselves in patterns there are chains with the point of one cell adjacent to that of the next or they may form rosettes The easiest way of demonstrating false sickling is by adding to a drop of fresh blood on a slide a few mg each of fibrinogen and of thrombin stirring with a match-stick, and then pressing down a cover glass.

The Scriver Waugh technique will show up true sickling if present, after not more than twenty four hours, provided that the leucocytes retain a certain amount of metabolic activity If the preparations are kept longer than this, changes in the composition of the serum are liable to cause false sickling Repeated tests on the same specimen may then yield varying results In our opinion this is what happened in the preparations of Caminopetros Agglutination, especially with anti Lewis sera may also give rise to an appearance resembling false sickling

Figs 1 and 2 show the difference between the two types of sickling Fig 1 taken from Huck (1923) shows the above-described features of true sickling whereas fig 2 from Dreyfuss et al. (1951) shows those of false sickling It was only through the generous attitude of Dr. Dreyfuss that we were able by repeating tests on Yemenite Jews previously tested by him both by incubation and by chemical tests to work out fully and to our own satisfaction the differences between

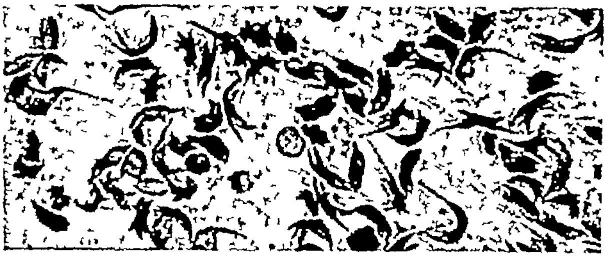
Fig 1—True sickling (Huck 1923)

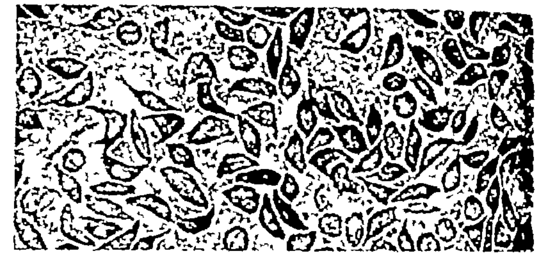
Fig 2—False sickling (Dreyfuss et al 1951)

these two types of "sickling" (Dreyfuss, Ikin, Lehmann, and Mourant 1952) Though it is desirable that all cases of sickling should be confirmed by the chemical reduction method, simple anaerobic incubation is almost equally reliable, provided that it is not continued for more than twenty four hours, and that the observer is familiar with the morphological distinctions between true and false sickling Thus the abnormally shaped cells from deer blood, figured by Gulliver in 1840 and reproduced by Singer (1951), are probably not true sickle cells as suggested

One of us (H L), in scrutinising past reports on sickling in the light of these new experiences, has become suspicious of his own findings in two African tribes which were part of a large number of observations made in Uganda in 1948–49 (Lehmann and Raper 1949) In the Kakwa tribe an original sickle-cell trait incidence of 12% was found to be increased to 25% by leaving the preparations overnight, but the increase was entirely due to the appearance of what are now recognised as false sickle cells In the Bakonjo tribe samples from some individuals (taken by finger pricks) were examined after they had been working in a salt lake, and all the members of this group, otherwise unselected, showed the false type of sickling This increased the reported incidence for the tribe as a whole

TABLE I—ABO BLOOD GROUPS OF GREEKS

Blood group	No observed	Frequency observed	Frequency expected	No expected
O	44	0 400000	0 404017	44 508
A_1	38	0 345454	0 325563	35 812
A_2	8	0 072727	0 087619	9 638
B	15	0 136364	0 130875	14 396
A_1B	2	0 018182	0 038793	4 267
A_2B	3	0 027273	0 012534	1 379
Total	110	1·000000	1 000001	110 000

Gene frequencies

O	0 636095
A_1	0 202727
A_2	0 065500
B	0 095678
Total	1 000000

Incidence of Sickling in Greece

In view of the divergent views expressed on the incidence of sickling in Greece as a whole, and of the possibilities of error which have been shown to exist, especially by the controlled tests on Yemenite Jews, it was clearly desirable that Greeks from all over the country should be tested for sickling by chemical means We therefore examined the blood of 110 Greeks, 50 born in Athens and 60 in other parts of Greece, but not from Petromagoula These people were unrelated to one another, and, apart from being available in Athens, they could be regarded as unselected

Samples were sent to London by air in three batches They consisted of capillary blood enclosed in sealed glass tubes, and each batch was accompanied by one or two samples taken from known Greek sicklers who [illegible], not included in the series All the samples [illegible] by incubation with sodium metabisulphite (Daland and Castle 1948) and with sodium hydrosulphite (Williams and Mackey 1949) The known sickle- bloods all yielded positive results, whereas the 11 unselected samples were uniformly negative

Blood-groups in Greece

In view of the paucity of data on Greek blood group in general, and of the implications, discussed below of both sickling and Rh groups on possible A connections, it was decided to determine the ABO Rh, and MNS blood groups of all the specimens A sickling tests had been carried out at St Bartholomew's Hospital, the specimens were transferred for grouping to the Blood Group Reference Laboratory

Samples were tested with anti-A, anti B, anti-C anti c, anti D, anti E, anti M, anti-N, anti-S, and anti Henshaw Samples positive with anti A were further tested with anti A_1, positives with anti E were tested with anti e, specimens negative with anti D in saline solution were submitted to an indirect antiglobulin *test with "incomplete" anti D in order to detect* D^u antigen if present

The results of the tests are set out in tables I–III. Gene frequency calculations were made by Dr Ada C K by the methods briefly described by Allison et al (19 which will be more fully described by Mourant (1953)

Discussion

Considerations of independent mutation apart, the absence of any example of sickle cell trait among 110 unselected Greeks makes a large Negroid or Ved doid component in the general population unlikely Even the presence of sickling locally at Petroma (Choremis et al 1951) does not necessarily imply an African connection, since a high frequency of this trait has now been found in Veddoids in India (Lehmann and Cutbush 1952a and b) and Arabia (Lehmann and Ikin 1953) On the other hand, the frequency of the cDe (R_o) chromosome is 4 6%, which is higher, though not significantly so, than in northern and central Europe and nearer to the frequencies found in several other Mediterranean lands, where it is almost certainly due to a small African component in the population It thus remains possible that the sporadic cases of sickling in the Mediterranean area have a similar origin, though they may have come from Asia (Lehmann 1953)

TABLE II—MNS PHENOTYPES OF GREEKS

Phenotype	No observed	Frequency observed	Frequency expected	No expected
MMS	23	0 211009	0 198207	21 605
MsMs	9	0 082569	0 094782	10 331
MNS	29	0 266055	0 280156	[illegible]
MsNs	25	0 229358	0 210434	[illegible]
NNS	11	0 100917	0·093818	[illegible]
NsNs	12	0 110092	0 116801	12 731
Total	109	1 000000	0 999998	[illegible]

Chromosome frequencies

MS	0 233417
Ms	0 307867
NS	0 116955
Ns	0 341762
Total	0 999999

Letters to the Editor

CHILDREN IN HOSPITAL

SIR,—Dr Mac Keith, in his article last week on the anagement of children in hospital before operation als with a subject of great importance to plastic rgeons and others concerned with the treatment of ngenital deformities needing repeated operations The ue facts about the efficacy of current pre anæsthetic gents for children are less reassuring than he implies

If the objective is a child quiet and amnesic for the hole of the induction period then it is my view that is objective is still not attained in most hospitals here is more involved than the choice of pre anæsthetic gent. Both oral sodium pentobarbitone ('Nembutal') d rectal thiopentone are often successful. But the more ten the child is subjected to anæsthesia, the less liable these agents are Their success is largely deter ined by the skill of the ward sister in their adminis ation and in the general arrangements in the children's ard for preparing children for operation

It remains my experience over a number of years, at I hear signs of struggle and crying from the anæs etic room in a big proportion of the children on whom do operations. There are some hospitals where this is ot so In these the ward arrangements are particularly od There are others where it happens more often an not.

There is not the least doubt that the premedication of ildren is one of the most important unsolved problems modern anæsthesia—if by a solved problem we mean ne whose solution is successfully applied in most ospitals most of the time

I can amply confirm Dr Mac Keith's account of the arm which can be done in the pre anæsthetic period to hildren, and I have often had to modify an important rogramme of repair because of the severe emotional ffects which the stress of the pre-anæsthetic battle has n the child. For any child to go conscious to the næsthetic room smacks of the surgical Middle Ages.

London, W 1 PATRICK CLARKSON

SIR,—Dr Mac Keith's excellent paper lacks a summary his might well be: Treat children as adults and they re easy *treat them as children and everyone suffers*

Children are not naturally afraid of anything even ospitalisation and anæsthesia unless a fear has been reviously instilled in them One way to ensure the onfidence of the child is for the anæsthetist to conduct "preoperative round with the children showing them he operating theatre anæsthetic room &c The con alescent children will explain the functions of these laces to the new children and a healthy pride in not eing a baby' is nurtured in everyone. Such a round onducted weekly, is well worth the anæsthetist's ime and saves many a stormy induction

But I cannot agree with Dr Mac Keith's views on the remedication of children All sedatives induce a state imilar to mild intoxication with alcohol and whereas his state is accepted by the adult it may produce terror nd a 'nightmare state in the child because of gnorance Children should reach the anæsthetic room rior to surgery either fast asleep or in complete ossession of their faculties

The Hospital for Sick Children,
Great Ormond Street,
London, W C 1

B G B LUCAS
Consultant anæsthetist.

SIR,—Nothing could be more commendable than the urpose behind Dr Mac Keith's article advocating hat children in hospital for operations should be so anaged as to inflict on them the minimum of psychic rauma He emphasises that one of the three main actors producing ill effects is induction of anæsthesia nd in this connection uses such expressions as forced sleep ' feel themselves slipping away under the anæsthetic' and the doctor personally should lead the child from the mother to the operating room These expressions produce in the mind of the reader a picture which one can only hope does not truthfully represent *what goes on at Cameron's hospital in 1953*

It should surely by now be taken for granted that except under exceptional circumstances all children should be given such preoperative medication as will ensure in most cases at least that they will have no memory at all of their visit to the theatre or of induction, thereby entirely eliminating one of Mac Keith's three traumatic factors This can be done of course in a number of ways without resorting to rectal administration which many children dislike quite as much as *conscious induction In the case of tonsillectomy* which represents by far the greatest number of children's operations, I am at present engaged in following up some hundreds of cases after return home from hospital where they are given sodium pentobarbitone (Nembutal) by mouth on a more or less dose-for-age scheme without individual consideration This is not ideal but is practical The investigation is not yet complete but the results to date show that between 90 and 95% of the children under 10 years of age have no recollection of having had an anæsthetic at all, so far as their parents can tell, and that on return home 96% show no nervous upset which is noticed by the parents

This result seems at least good enough to eliminate the necessity of talking to children beforehand about their anæsthetics, except to say that they will be given a drink and will then go to sleep In individual cases in ideal conditions such as nursing home practice, where more time and a constant staff are available, and induction can be carried out in bed, there should of course be a virtual guarantee that the child will have no consciousness of having been to the theatre or of having had an anæsthetic

In fact, the anæsthetist should not do a great deal to allay the child's fears he should see that the *causes of them as far as he is concerned are eliminated* altogether

Windsor DOUGLAS BELFRAGE

INCISION FOR ACUTE APPENDICITIS

SIR—In their article last week Mr Ewing and Mr Monro by implication once again raise the question of drainage following appendicectomy for acute appendicitis. A main advantage of the muscle-cutting incision they find is its suitability for drainage, while Battle's incision is condemned amongst other reasons because of its unsuitability for drainage

This argument seems to me fallacious since the peritoneal cavity should never be drained following appendicectomy whatever the degree of peritonitis It is generally conceded that drainage can do no good and may lead to infinite harm encouraging the formation of fistulæ and adhesions Though it might seem reasonable to drain the subcutaneous tissues when a perforated gangrenous appendix has been removed and free pus is present, I have found this disappointing since often enough a superficial abscess will point perversely at the opposite end of the incision

Many surgeons choose Battle's incision for appendicectomy Retraction *of the rectus muscle should cause no injury and, as Ewing and Monro point out* the incision is valvular and gives the most direct access. Infection of the rectus sheath is a theoretical disadvantage which is not borne out in practice ecause adhesions rapidly seal the layers of the to the muscle Battle's incision ensures t nd 12th thoracic nerves are seen and so submit that hernia formation follow A postoperative hernia is equally rare otherwise identical, incisions—the pararectal approach to the lower end of ureter, and McEvedy's repair of femoral hernia

For these reasons I maintain that Battle's incision should continue to have the sanction of the standard works on operative surgery

Salisbury Hospital Group PHILIP SHEMILT

SIR,—I think that those who have to deal regularly with acute abdominal conditions will endorse the opinions expressed last week by Mr Ewing and Mr Monro

After three years in the tropics, despite the wider range of differential diagnoses, I remain strongly in favour of the McBurney type of approach (with a transverse skin incision), sited in accordance with the physical signs, or Kocher's modification (Rutherford Morison) This applies unless a pelvic location is suspected Naturally, where there is genuine doubt the paramedian incision has a place , but then the operation is a " laparotomy " rather than " for acute appendicitis "

Many of my patients were seen later than is usual in this country *In 12 of the last 25 consecutive cases the appendix* had already perforated In many an abscess had localised, or, in earlier cases, fragile adhesions were forming , and approach through the unaffected part of the peritoneal cavity would have seemed indefensible No one would deliberately approach an appendix abscess by way of the unaffected peritoneal cavity, and I consider that all cases of acute appendicitis should be thought of as potential abscesses , and if operation is performed, the approach should be the most direct route from the surface My experience with antibiotics in intra-abdominal infections has not led to any modification of this view

In commenting on the frequency with which the acutely inflamed appendix is approached in this country by the midline or the paramedian routes, Ewing and Monro state that these approaches have the sanction of many of the standard works on operative surgery On taking a random selection of textbooks from the shelves of a medical school library, I did not find this confirmed, although it may be true of some of the more specialised works Of six textbooks,[1–6] one [5] suggests that the McBurney incision is out of date except for opening an appendix abscess , but the remainder express views which do not deviate from those of Ewing and Monro

London, S E 1 MICHAEL FLINDT

ASPHYXIA IN THE NEWBORN

SIR,—Dr Noel Jackson in his letter (Oct 17) quotes me as follows

> " Writing on artificial ventilation of the lungs, Professor Pask [7] evidently prefers efficient artificial respiration to inadequate spontaneous respiration, for he remarks ' Positive pressure ventilation can be carried out without causing *disturbance in the cardiovascular system* ' "

With the first part of this sentence I agree, but the quotation from my letter seems to have changed rather strangely, for it ran as follows

> " I believe that *many physiologists will be surprised to learn* that positive pressure ventilation can be carried out *at all* without causing *some* disturbance in the cardiovascular system "

Dr Jackson's diagram and explanation of his apparatus worry me If the surgical rubber glove really functions as a rebreathing bag, I think it is too big Furthermore, babies who are called upon to breathe or rebreathe through intravenous needles have my sym-pathy, even though the needles be " fairly large " Th diagram suggests connecting the babe directly to th oxygen supply I think this is unwise and leads to risk of burst babies

Department of Anæsthesia,
Royal Victoria Infirmary,
Newcastle upon Tyne E A PASK

EPIDEMIC VOMITING

SIR,—I read your annotation of Oct 3 and the let by Dr French (Oct 10) at a time when cases of condition were occurring in my practice. They hav increased in number, and I myself became a 2 days ago

Usually there is fatigue, headache (in my own case and in the tissues of the scalp), general aching, and hot cold feelings, followed within a few hours or up to a day two by bilious vomiting Temperature varies from norm to 104°F and the pulse is usually rapid. Occasionally there abdominal pain and slight giddiness, but never true vertig There is no sign of liver tenderness or jaundice, and meningeal signs , but, as in Dr French's series, one appeared which *may or may not* have belonged to the group This was in a woman who developed, after the onset, a 7th and 11th cranial nerve palsy and herpetic on the left side of the palate In the occasional infections the interval between cases has been about 5 da The length of the illness varies from 1 to 7 days.

Ilford, Essex R N C SMITH

CONTRACEPTIVE TECHNIQUE

SIR,—Dr Maung Sein's letter of Sept 26 starts well enough on firm ground but ends in a morass right and proper that he should quote the Americ figures and the immense amount of work done in th country on follow up studies , but this controversy the relative over all effectiveness and acceptability the combined methods of contraception (cap or sh plus jelly, paste, or suppositories) versus the methods (jelly or paste or suppositories or condom alone) is a very old one and still rages Unfortunate simply to quote pregnancy rates means very little, is necessary to know quite a lot about the back of the various series before it is possible to judge wh the comparison is a fair one (e g , number of nullip age range , previous fertility , duration of use , so economic, educational, and religious background, so forth) Still more unfortunately one cannot al discover these important facts even in the original paper, and this applies to a large extent to papers published on ' Preceptin '

In any case all this talk about pregnancy rates is confusing the original issue I was not concerned pregnancy-rates but with one particular patient, a hi fertile, sick woman, most willing to coöperate with medical advisers in every way , in fact she coöpera with them so well that she used preceptin when was advised to do so, with disastrous conseq having previously used a combined method with suc Dr Maung Sein will have a job to convince me *all other things being equal*, it is possible to offer a as complete protection against pregnancy by giving a paste or suppository to use alone as by providing with a mechanical barrier to prevent direct insemin of the cervix plus a chemical one to kill the sp This is not to deny that preparations such as and various suppositories have their place in con tion, and, as I said in my letter of Aug 15, this paste will in time find its correct level of use It will undoubtedly be of value in the first of Dic categories but I very much doubt if it will be *the* an for many in the other three

The last part of Dr Maung Sein's letter had be left unanswered—not because it is unanswerable because it starts a number of irrelevant hares

Crediton, Devon MARGARET HADLEY JAC

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1 Bailey, H , Love R J McN A Short Practice of Surgery London, 1952
2 Handfield Jones R M , Porritt, A E The Essentials of Modern Surgery Edinburgh 1951
3 Illingworth C F W Textbook of Surgical Treatment. Edinburgh 1947
4 Maingot. R. Abdominal Operations London, 1940
5 Romanis W H C Mitchiner P H The Science and Practice of Surgery London, 1952
6 S The Art of Surgery London, 1937
7 1953 i 1048

THORIUM DEPOSITS IN THE LIVER

Sir,—I welcome last week's article by Dr Berenbaum nd Dr Birch who summarise recent reports on the ore dangerous side-effects of Thorotrast and empha se the difficulty in tracing the cause of death in patients ho received one single injection of thorotrast about 20 ars earlier

Before thorotrast was marketed I carried out extensive periments on rabbits and rats which were observed for months or more [1-3] The results of these investigations ere summarised in an answer to your annotation on e danger of thorotrast 15 years ago [4] Most of the thological reactions following thorotrast injections ere known already in 1032 (the year when thorotrast as marketed) and although the observation time in y series was far too short for such changes as aplastic emia and malignant tumours to have appeared even those early studies due mention was made of the ssibility of these complications At the same time a arning was sounded against the use of thorotrast in an Perhaps this warning was instrumental in reducing e number of fatalities on the Continent

London, W 1 Z A LEITNER

CERVICAL SPONDYLOSIS SIMULATING MOTOR-NEURONE DISEASE

Sir,—I have read with interest the article on cervical ondylosis by Dr Liversedge and his colleagues in ur issue of Sept. 26 It strikes me that some of the nfusion in the early diagnosis of their cases might have en avoided if the jaw jerk had been recorded I can e no mention of this having been done Surely a ormal jaw jerk in the presence of otherwise brisk ndon reflexes would cause one to hesitate in the iagnosis of motor neurone disease ?

Johannesburg South Africa ROY MORRIS

CHRONIC BRONCHITIS

Sir,—Dr Oswald and his colleagues (Sept 26) have iven us some important clues in the search for the cause f chronic bronchitis. Even though there are still many aps in our knowledge it is essential that we should pply the facts we already know Dr Oswald emphasises he importance of the quality of the inspired air Although e can hardly hope to affect our damp cold winter imate there are several ways in which the chronic ronchitic can be given better air to breathe.

Smoking is undoubtedly one of the chief irritants in hese patients. It is unusual to find one who fails to otice distinct improvement in his symptoms when he as stopped this habit. I am surprised how rarely atients have been advised about smoking by their wn doctors The majority of patients with chronic ronchitis will stop smoking provided they are told f the importance of doing so in strong enough terms. consider tobacco is poison for a chronic bronchitic nd I tell him so

Last winter's fog killed 4000 people in London, the ajority of whom had chronic bronchitis In the late ar the remote chance of a gas attack produced elaborate nd expensive precautions on a wide scale yet we main relatively complacent in the face of these recurrent s-attacks, which kill many of our citizens yearly ong-term plans to lessen air pollution are essential ut until they are effective the patient with chronic ronchitis should be given similar protection from fog that which the war time civilian was given from oison gas. The sufferer from chronic bronchitis usually ays at home during fogs, knowing his risk of relapse Could not a room in his house be made fog proof just as each civilian learned to make one room gas proof in the war ? Civil defence authorities would probably be willing to help and advise He should also be advised to wear a light mask, at any rate when having to go out of doors

It is time that we paid more attention to the purity of the air which our patients breathe and endeavoured to prevent them from consuming their own and everybody else's smoke

Central Middlesex Hospital,
London N W 10 KEITH BALL.

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[1] Leitner Z. A *Fortschr Röntgenstr* 193[illegible] 46 47
[2] Bucky G., Leitner, Z. A *Ibid* 1932 45 56
[3] Anders H E., Leitner Z A *Klin Wschr* 1932 11 1097
[4] Leitner Z. A. *Lancet* 1935 i [illegible]8

THE PLACEBO

Sir,—Both the contributors on this subject in your issue of Oct 17—Dr Barham Carter and Dr Handfield-Jones—have omitted to ask the highly pertinent question Who needs the placebo ?

Our patients do not demand placebos I have yet to meet the patient who asks : Doctor may I have a placebo an inert inactive substance ?' Patients ask us for help though often in an inarticulate way difficult to comprehend yet it is our task to try to understand the patient's needs For instance Dr Barham Carter's patient who had a urinary infection probably venereal in origin, and who ten years later was still on methylene-blue was obviously not freed from anxiety about his illness and needed more treatment, not necessarily with methylene blue But again obviously methylene-blue for ten years was better to him than nothing

If the doctor's inner hearing is not acute enough or if his understanding of the patient's need is barred by bias or prejudice, or if the patient arouses anxiety or guilt within the doctor, then the doctor only too often has to prescribe a placebo because he needs it for his own reassurance And this is the true function of the placebo It does not serve the patient's, but the doctor's need whatever the excuse may be with which it is prescribed.

The term 'placebo then needs re-definition The definition given by your contributors (an inert drug given to please or satisfy the patient) is contradictory in itself Firstly no drugs not even water or salt are truly inert secondly all treatment is given to please or satisfy the patient What greater pleasure or satisfaction could we give the patient than to free him from disability or illness ?

Treatment by a placebo is rightly contrasted to scientific treatment—that is to treatment that is fully understood in its implications but many forms of treatment which are considered scientific in themselves such as electro-shock insulin shock or antibiotics, may well be given as placebos as much as the reassuring pat on the shoulder and the red tonic

It is not enough (as Dr Barham Carter thinks) to take an adequate history or make an adequate physical examination We must also try to understand the inner needs and longings of our patients, or else all well meant treatment with fine names after high-sounding diagnoses will be a placebo for the satisfaction of our own needs.

The people that come to see us for help are ill and we all retreat in illness, in ill-adaptation to a state of infantile narcissistic dependency where we long for satisfaction and comfort by medicines diets, cooling drinks soothing broth as if illness aroused memories of early infantile dependent days when mother's breast the bottle, the dummy or our own thumb gave us similar oral satisfactions

Cabot's remark (quoted by Dr Handfield-Jones) that babes are not born with the desire to take a drug for every symptom is quite wrong The babe needs very much oral satisfaction for his symptoms, and the eternal babe within us, that comes into the forefront in illness very often needs satisfaction by mouth. Such longings have to be considered in scientific treatment, too, or else the scientific view would be incomplete We need not feel ashamed or guilty because, in full knowledge of their effect, we have prescribed preparations which have no easily definable pharmacological action upon an isolated organ or system

Let us define then (and reject) any treatment that is given without the doctor fully knowing and understanding what he does by treating the patient—as a placebo for the doctor

Southall, Middlesex. M B CLYNE

SIR,—Dr Barham Carter (Oct 17) is wrong, according to all principles of psychotherapy, to give psychoneurotic patients a placebo as "a material sign to establish confidence so that they will benefit from the real helpful psychotherapy that follows" Once it has been established that the patient does not require medicinal treatment, he will create in this patient, not confidence, but the conviction that there is some medicinally treatable condition If the patient already believes that "words can't help my trouble," he makes his job of giving the patient effective psychotherapy almost hopeless The exhibition of placebos is a regression to pre Freudian days It could even culminate, as I have experienced, in this trend of "reasoning" the patient will not accept the psychogenic basis of his disorder, therefore, if I help him to convert his psychoneurosis into an organ-neurosis, I can treat this by drugs If we are dealing with a somatopsychic disorder—e g, asthma mucous colitis, duodenal ulcer, neurodermatitis—palliative medicinal treatment is, of course, indicated, and this should be fully explained as palliative Drug treatment in psychiatry is also indicated in the well-recognised and defined syndromes—e g, vegetative imbalance or concomitant emaciation—but again this requires full explanation to the patient, as to what it is intended to produce or effect But placebos ? No !

Winterton Hospital,
Sedgefield Co Durham D J SALFIELD

POSTURE, BACKACHE, AND HEALTH

SIR,—In your issue of Oct 17, Mr W E Tucker discusses human reaction as illustrated by the manner employed by a person in his standing and sitting Now, in standing and sitting, as in all the variations of human reaction, the relationships between the various parts of the person are guided and controlled by means of sensory communications known medically as kinæsthesia The way a person adjusts himself as a whole depends upon how well kinæsthesia works, and this again depends upon how the communicating mechanisms are adjusted When the means of communication are badly adjusted the standard of kinæsthetic guidance is low, when they are well adjusted, the standard is high Mr Tucker must be aware that Rudolph Magnus demonstrated that the adjustment of the animal as a whole enabling the sensory and motor communicating mechanisms to operate at their best and, therefore, in a reliable way, was an adjustment which he showed was associated with a certain relativity of the head to the neck Sherrington also acknowledged the importance of the head neck relativity in connection with knowing how to control human reaction In the light of the views of these great experimenters, it must be clear that where a person does not react in accordance with a principle enabling him to use the psycho-physical mechanism or self in a way associated with a control over the relativity of the head to the neck ensuring a rising standard of kinæsthetic sensory appreciation, he is bound to do injury to the working of the self and, therefore to

One of the consequences of failing to observe th principle is that we form wrong beliefs about how th self works and are led along roads to knowledge whi are misleading The burden of retracing our steps alo these wrong roads grows the greater the longer w postpone the admission that wrong means will neve enable us to gain the best possible control over h reaction in its many and complex variations

Bolton, Lancs. MUNGO DOUGLAS

PERIODIC MEDICAL OVERHAUL

SIR,—Sir Adolphe Abrahams (Oct 24) considers that th purpose of the periodic medical overhaul is to the patient *when well* If by "well" he means health then by definition the medical overhaul will reve nothing If by "well" he means that the patient sa he feels well, many diseases are symptomless in th early stages and many otherwise sensible people some symptoms—e g fatigue, cough, obesity—as Their statement that they feel well does not mean th are healthy

My criteria for periodic medical overhaul are it should be done at appropriate intervals and that should be thorough The presence or absence of s is immaterial

Reigate Surrey ERNEST H CAPEL

HYPERTHYROIDISM IN CRETINS

SIR,—Dr McGirr and Dr Hutchison (Aug 22) sa that, in their opinion, the terms hypothyroid, euthy and hyperthyroid should continue to refer to the clin state of the patient and should not be used to refer to the functional state of the thyroid gland

I have observed [1] an endemic cretin with these func tional thyroid data

Basal metabolic rate (B M R) + 18%, protein bo (P B I) 8 9 µg per 100 ml ; serum protein (Pullfrich) 7 per 100 ml, blood cholesterol 105 mg per 100 ml, iodine uptake of the thyroid 87% after 2 hours, 81% 24 hours, follicle stimulating hormone in urine + 10, mouse units per 24 hours (Gorbman's method), pregnan 4 5 mg per litre (nearly 15 days after previous recurrence)

This patient received 20 mg of thyroid stimulating (T S H Armour) daily on three consecutive days, and this we obtained these values B M R + 30%, P.B.I 9 25 per 100 ml, blood cholesterol 93 mg per 100 ml

These changes show a ready secretion response of thyroid to treatment with T S H and a ready response to the increase of thyroid secretion

Recently in our hospital thyroidectomy was done non endemic goitrous cretin, whose thyroid fun data were

B M R + 11%, P B I 9 11 µg per 100 ml, thyroid of I^{131} after 1 hour 28 8%, after 24 hours 34 1% (H ratio 60%), blood cholesterol 133 mg per 100 ml logical examination showed many areas with indication hyperfunctioning adenoma

Why should we not call these patients "hy thyroid," as we call all other patients with such chemical data ? Of course we do not judge these pa to have Basedow's disease

Some workers suggest that the cretins we have cribed were probably hypothyroid in their early y and became hyperthyroid later

We answer

1 Nearly all endemic cretins we have studied showed high B M R a high I^{131} uptake, a high conversion rate, forming of labelled thyroxine, and a low P B I But P B I value was never as low as in true hypothyroidism (average value in 21 patients was 4 54 µg per 100 ml)

2 We do not believe that their high radio iodine is due to a low iodine availability, because normal people the nurses eating the same food, have a normal thyroid u

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1 Costa A *Rass biochim sci* July, 1953, p. 189

We cannot admit that a thyroid so insufficient as to cause ere signs can later correct spontaneously and so frequently

We think we have proved that endemic and non-endemic tins can be sometimes hyperthyroid On the other hand fact that their thyroid is failing to produce or to liberate ficient hormone to meet the needs of the tissues is still proved

According to us views on the pathogenesis of cretinism ght to be revised; these patients should not be considered othyroid because of their goitre or some functional airment of their thyroid or because they seem to hypothyroid

Mauriziano Hospital,
Turin Italy

A COSTA

THE DRUG BILL

SIR,—Since I entered general practice I have con entiously learned the official names of drugs and have scribed *National Formulary* preparations for the vast jority of patients, under the impression that by ing so I was helping to economise I have argued th patients who have been used to a proprietary ug and I have insisted on their accepting the inferiorly rketed product in cases where I now find it would ve been more economical to comply with their sonable request

How many other reputable manufacturers I have ghted directly or by implication I do not know t as a general practitioner I beg their pardon and ure them that if in their circulars, they give a clear tement that their product is as economical as the F preparation in total cost I shall try not to make same mistake again

G P

SPLENECTOMY IN ACUTE IDIOPATHIC THROMBOCYTOPENIC PURPURA

IR—At the surgical congress held in Berlin in 1923 d again in 1924 I expressed for the first time the nion that one should strictly discriminate from the ndpoint of ætiology and splenectomy between acute d chronic idiopathic thrombocytopenic purpura (I T P)[1,2] My contention then was based partly on my erience in Schloffer's clinic in Prague, where on the ommendation of Kaznelson the first splenectomies re performed for I T P and partly on the first 20 blished cases and 4 additional cases of my own at the gical clinic in Kiel Of these 24 cases, 4 were of the te type and of the latter only 1 survived splenectomy n 1 of the 3 unsuccessfully treated acute cases I cribed extensive necrosis of the vertebral bone rrow I attributed the thrombopenia to this finding ch was later confirmed by other workers—for example midt in Würzburg Eugene Fränkel in Hamburg l Ghon in Prague (personal communication)—but this on was the subject of controversy at the conference of German Pathological Society in 1927 No findings ilar to mine have been described since

y recommendation to exclude acute cases of I T P m splenectomy was generally adopted, and my clinical ervations confirmed, till Anschütz[3] rejected my views d advised early splenectomy in acute cases, on the umption that they differed only quantitatively and qualitatively from the chronic cases He admitted ever that the operative mortality in the acute group s as high as 70–80% Nevertheless many textbooks of matology and medicine nowadays adopt my view ht and advise against splenectomy in the acute form I T P This view is supported by the recent studies of fanini and Dameshek,[4] who suggest that it is now sible to recognise certain significant differences in the immunological mechanism between 'acute and chronic" types of I T P They also say that an immediate result of these findings has been that of emphasising the necessity of the careful assessment of the clinical and laboratory features of each case of I T P with particular reference to its acute or chronic nature This has considerable bearing on the decision whether and, if so when splenectomy should be done' It seems that these studies vindicate my opinion, expressed thirty years ago that acute I T P should not be treated by splenectomy in contrast to the chronic type which usually responds to this operation

One aspect of the purpura problem does not seem to be clarified by the latest work—namely, why females are predominantly affected I used to explain this fact on the basis of the periodical changes that take place in the female vascular endothelium—changes which may be caused by toxins perhaps Schick's menotoxins, and which render the endothelium more vulnerable to other factors that operate in both sexes I wonder whether this theory is still tenable

Kowloon Hong Kong

D ENGEL.

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[1] ngel, D *Arch klin Chir* 1923 126 160
[2] ngel, D *Ibid*, 1924 129 663
[3] schütz W *Beitr klin Chir* 1927 142 1
[4] efanini, M, Dameshek W *Lancet* Aug 1 1953 p 209

TREATMENT OF RHEUMATOID ARTHRITIS WITH PHENYLBUTAZONE

SIR,—Since our paper appeared in your issue of June 20 1953 Mr R G Carpenter F.S.S has drawn our attention to an error in the value of χ^2 in tables I and II Values of χ^2 should be:

Table I: χ^2 (with 3 degrees of freedom) = 12·77 $0{\cdot}001 < p < 0{\cdot}01$
Table II χ^2 (with 3 degrees of freedom) = 7·07 $0{\cdot}05 < p < 0{\cdot}1$

Thus whereas the subjective assessment gives a comparison highly significant in favour of the drug the *objective assessment shows only a suggestive difference* between the drug and control groups. As we laid more stress on the subjective than on the objective assessment we do not consider the validity of our conclusions to be substantially diminished

DERYK FREELAND
GEOFFREY STOREY
MICHAEL THOMPSON

Department of Physical Medicine
London Hospital E 1

HYALINE MEMBRANE IN THE NEONATAL LUNG

SIR,—I read with interest the article by Dr Claireaux (Oct 10) which confirms the importance of hyaline membranes as a factor in neonatal death I would like to make two comments Firstly aspiration of amniotic fluid by a fœtus in utero produces uniform partial expansion of all alveoli Should such an infant survive for a short period after birth sections of the lungs show inspired air pressing squames and debris of the amniotic fluid against the alveolar walls and the individual squames can usually be identified. Dr Claireaux and previous workers agree that the predominant site of the hyaline membrane is not the alveolus but the alveolar duct I think these observations make it unlikely that any constituent of amniotic fluid plays a major rôle in the formation of these hyaline membranes Secondly the hyaline membrane produced experimentally in the rat was the result of the intratracheal injection of 1 ml of concentrated hyaline material and appears to bear little relationship to the postulated aspiration of normal amniotic fluid by the fœtus

In his comments last week Dr Emery does not amplify his belief that intrapulmonary vascular changes are major factors leading to formation of hyaline membrane but this theory does not appear to account for the nuclear remnants found in some lungs by Dr Claireaux and myself It may well be that hyaline membranes found in diverse conditions are due to more than one pathological process.

Memorial Hospital,
Darlington

J TREGILLUS

Medicine and the Law

Praise or Blame at Inquests

On Sept 23 a coroner's jury at Guildford, having inquired into a fatality caused by an accident to an electric train at Guildford Station, returned a verdict of accidental death and added a rider exonerating the motorman from blame At a subsequent inquest at Guildford[1] the coroner spoke of this rider as unfortunate and reminded the jurors that they must not introduce into their verdict anything which may tend to decide the question of civil liability

The new Coroners Rules, which came into force on March 1 last, are quite clear upon this point and, though already familiar to coroners, may need repeated emphasis in any summing up to a jury The effect of the rules is that the proceedings and evidence at an inquest must be directed solely to ascertaining (*a*) the identity of the deceased, (*b*) how, when, and where he came by his death, (*c*) the persons, if any, who (if the findings warrant it) might be charged with murder, manslaughter, or infanticide, and (*d*) the particulars required for registration of the death "Neither the coroner nor the jury shall express any opinion on any matters other than those referred to" in the foregoing provision, though an exception may be made for any recommendation designed to prevent the recurrence of similar fatalities "No verdict," moreover, "shall be framed in such a way as to appear to determine any question of civil liability"

This restriction follows the recommendation of the council of the Coroners Society in the draft Rules of Procedure of 1937 Chapter VII of the report of Lord Wright's Committee had drawn attention in the previous year to the apparently growing practice whereby interested parties made use of an inquest in order to elicit facts which might bear on civil liability but which were strictly irrelevant to the issue before the coroner The committee had been told that parties were frequently represented at inquests with a view to securing a rider exonerating the person concerned or placing the blame on someone else The advocates, said a witness from the Law Society, seemed to be turning the coroner's inquest into a county court or High Court and raising small questions of negligence which might bear on the award of damages, thus prolonging the proceedings at an inquest and covering unnecessary ground A representative of the county chief-constables quoted a coroner as saying that inquests were "becoming happy hunting-grounds for gentlemen who come here to pick up material on the chance of getting damages out of one party or another"—clearly an abuse of the coroner's court

As the Wright Committee observed, the coroner's court is not equipped for such an inquiry The Home Office had cited a case in which a coroner had given directions to a jury on a question of workmen's compensation law—whether a fatal accident did or did not arise "in the course of the workmen's employment" The Ministry of Pensions had given evidence of inquests being allowed to discuss the extent to which war service had contributed to the death In a subsequent chapter the Wright Committee laid similar emphasis on the need of avoiding verdicts or riders of censure or exoneration It was contrary to natural justice that persons might find themselves condemned in proceedings to which they were not parties and in which their conduct was not in issue

Medical practitioners who happen to be summoned as witnesses at an inquest will note the significance of the new rules They may be saved a protracted examination on some question of civil negligence

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[1] *Times* Oct 14

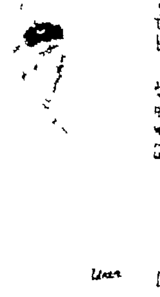
Obituary

ROBERT TENNENT

M.B Glasg, F R C S E

The death of Mr Tennent in Stirling on Oct 9 deeply affected a wide circle of friends

He was born in Strathaven in 1890 and received early education at *Hamilton Academy, of which he* a distinguished pupil From the University of he graduated with honours in 1914, a few months b the outbreak of the first world war, throughout he served in the Royal Navy He was granted to take the fellowship of the Royal College of Surgeons of Edinburgh and this he did in 1917 After the war he was appointed to the staff of the Royal Hospital for Sick Children, Glasgow, where he was junior to the late Mr Alexander MacLennan, whom he also assisted in private practice His appointment to the Victoria Infirmary soon followed, and there, after some years as first assistant to Mr R B Carslaw, he was given charge of wards in 1927 at an unusually early age Making this his chief interest and regretfully discontinuing his work at the Sick Children's Hospital, he entered into a period of very active hospital and private practice, terminated by resignation in 1949, the end of his long and association with the Victoria being forced upon his failing health



In 1924 he accepted the invitation to become surgeon to *Falkirk Infirmary*, and his connection this hospital was also a very happy one, he the responsibility and credit for the planning of Royal Infirmary which was opened there in 1932, was therefore understandable that he should *to do some work there even after his retiral from* in Glasgow

Tennent's work in the Victoria Infirmary earned him in Glasgow and throughout the West of reputation for work of the highest quality, in the fields of abdominal and thyroid surgery, in *latter he achieved particular eminence, and it is* table that he did not live to carry out his intention publishing his results Although he latterly tended be more circumscribed he was so much the surgeon that any new method received consider and underwent trial at his hands, he had been example, one of the first in this country to Harris technique for prostatectomy Above all, T was characterised by a dexterity and gentle hand which gave him results surpassed by few He surgeon who could make surgery look easy, and celerity, combined with a natural aptitude for made his life exceptionally full and busy

Tennent taught well and was for many years a lecturer in surgery to the university, and in his years examined for the final M B CH B Proba unofficial teaching which he did as an assistant gave him the greatest pleasure For many gathered round him on Saturday mornings a large of final year men, and his ward rounds then delight Many a student learned as much surgery his informal, anecdotal talks as from a series of sedate clinics, and these tutorials will live long memories of those who attended them He must been a most kindly examiner, and it is difficult to any candidate being other than at ease with him; it is equally difficult to believe that his intuitive ment of a man was wrong if he considered him a future doctor

In spite of all his activities, Tennent found many interests apart from his profession Angling his first love, and he knew intimately most of the his native country his friends were legion among untrymen in all walks of life. His love of country ings and country folk was exemplified by his wide owledge of Scots ballads, which his retentive memory abled him to recite freely, and it was another of his ots attributes that he could quote the Old Testament length and with accuracy.

Robert Tennent was a fine surgeon; he was also a e man, and this side of his character was most impres ve to those who were so fortunate as to be his friends. e was generous to a fault, and his help was always ailable to patient and colleague alike at no matter hat sacrifice of his time and energy. Many young men ve their start in general practice and surgery to the nselfish help given by him.

The second world war made increasing demands on m at a time when normally he might have been pected to begin to enjoy more leisure. These demands ere met in full but only at a cost, and in 1947 came e first signs of the vascular disorder which made it ecessary for him to modify his activities. Shortly after is he went to live in Dunblane and gradually made is severance from Glasgow well nigh complete.

He leaves a widow, three daughters and two grand ildren, of whom he was exceedingly proud. He will remembered with gratitude by many, with affection many, whether they knew him as the surgeon, the iend, or as both.

J. P. G.
R. G. H.

WILLIAM ELDON TUCKER

B.A., M.B. Camb., F.R.C.S.

Dr. Tucker died on St. Luke's Day, Oct. 18, at the e of 81, in Bermuda, where he had practised for nearly lf a century.

From Bermuda he went to school at Port Hope in nada, where he was a classical scholar and head of the hool. In 1891 he came to this country to study edicine at Caius College, Cambridge. He soon won fame the Rugby world, playing for Cambridge and England. ven in the 1920s many of the college servants remem ered his feats of strength, for he had gained the putation of being, among other things, one of the ongest men ever to be at the Varsity. He captained e Cambridge XV in 1894, the same year as the late M. Carey captained Oxford, and the result was a draw. th men played in the England team together with ch great players as A. F. Todd, S. M. J. Woods, and ank Mitchell, and were firm friends. It was a coin dence that Carey and Tucker were born on the same y, Aug. 17, 1872, the one in the island of Guernsey d the other in the island of Bermuda.

Tucker qualified in 1899 and held house-appointments St. George's Hospital until 1902, when he returned to muda and started in general practice. Before his ival only two major operations were known to have en performed in the islands. Through his efforts, wever, and those of the late Dr. Trott, several hundred jor operations were performed at the hospital each ar.

During 1914–19 he acted as surgeon to the Military spital, Bermuda. On one occasion, when a ship-load frost bitten West Indian troops arrived from the rth in winter, he performed about 150 amputations thin a month. As motor-cars for general use were permitted in Bermuda until 1947, he visited his tients either on horseback, bicycle, or horse-drawn rriage.

As a practitioner of the old school he was loved and spected throughout the islands. Although he was a n of strong personality and definite views, thanks to s gentleness and frankness he made few enemies but ny friends. In later life he became crippled with eo-arthritis, and in 1949 he had to retire from practice, t he bore his disabilities with a stout heart. The Royal llege of Surgeons of England conferred their fellowship him in April this year, and with great pride he made e journey over by air to receive the honour which put e seal on his full and useful life.

He leaves a widow, two daughters, and two sons, one whom is Mr. W. E. Tucker, F.R.C.S.

Sir EWEN MACLEAN

Sir William Fletcher Shaw writes:

I have a vivid recollection of seeing Sir Ewen Maclean for the first time when I was taken, as a visitor, to a meeting of the Representative Body of the B.M.A. in Liverpool during the stormy time of the Lloyd George National Insurance campaign. His tall, slim, gracious figure, with the long Scottish head and marked features and the pleasant clear voice, seemed almost boyish, but he knew his subject backwards, and had complete control of what might have been a very unruly meeting: if I remember rightly, it was after the Smith Whittaker resignation. I was much impressed, but little thought at that time how well I was to know him later. My first personal contact was at the end of the first war when I was elected a member of the Gynæcological Visiting Society. In this band of friends he was one of the leaders, always full of fun and ready to laugh at a joke against himself, an attractive after-dinner speaker who was popularly supposed to act up to the motto "Where I dines I speaks"; never ruffled, always kindly and friendly to juniors. I found his most attractive feature in his readiness to discuss any subject about which there was a difference of opinion—never didactic or blustering, always wishful to convince by pure reason.

It was this feature which made him so valuable to the Royal College of Obstetricians and Gynæcologists in its formative and early days. He was one of the four who formed the first committee to explore the possibilities of its foundation. In those days, perhaps, he contributed the least largely because so much had to be done by correspondence, and he never wrote long letters, at any rate to me, nor would he employ a secretary; but he attended every meeting and turned clear common sense on to every proposal. Towards the end of this formative period and during the first three years of the life of the college, when we were torn by personal dissension, he was invaluable. I had become honorary secretary and the recipient of stormy correspondence from all sides, often fearing that the next meeting would blow the fragile nursling sky high; my one anxiety was to have Maclean present, the one always to be relied upon never to lose his temper or to use an expression which would irritate either side, but talking horse sense until both sides saw it and the storm quietened.

He became president himself at a fortunate period for the college when his peculiar gifts had full play. Personal quarrels had now disappeared, and, even more important, under the presidency of his predecessor, Fairbairn, the friction between London and the rest was finally settled and the college was ready to bound forward again and to earn its charter and the title "Royal."

His gracious manner, attractive appearance, and able speaking, his love of people, and his large acquaintance with public men from his former position in the B.M.A. and through his brother Sir Donald Maclean, were just what the college required to bring it into public notice. During this period the Minister of Health, for the first time, formed a small advisory committee which Maclean was asked to join. Since then, whatever form this committee has taken, his successors as presidents have been members; but I always thought this first invitation was due as much to his personal qualities as to his office. So too he laid the foundations for the "Royal" and the charter, neither unfortunately arriving during his presidency—the "Royal" only two months after he had laid down office and the charter only in 1947 because the war intervened just as it was on the point of being granted. But they were really won in his time.

The three years of his presidency was perhaps the happiest period of my secretaryship; he was so easy to work with, never any personal rancour, all differences of opinion discussed in a friendly atmosphere and a *via media* found, no desire for personal aggrandisement, always the good of the college. We dined together in London most weeks and settled our line of action in the many problems which arose, and not once was there the slightest jolt to our friendly coöperation. During the five years of my presidency he remained on the council. This was the difficult period of the early war years with completely new problems and new contacts. He was a tower of strength on which I could rely, never usurping the position he had just vacated, always ready with shrewd helpful advice.

Others will write of his many other activities. I record merely what the college as a whole and what I personally owe to him. A great gentleman and a true friend.

Notes and News

FROM MYSTERY TO MASTERY

Of the five Heath Clark lectures on Man's Mastery of Malaria given this week at the London School of Hygiene and Tropical Medicine by Dr Paul F Russell, of the Rockefeller Foundation, the first was on Monday when Sir Neil Hamilton Fairley, F.R.S, presided over a large gathering Dr Russell admitted that his title was optimistic, for malaria still does immense damage to mankind, but he hoped it was not too exuberant the word mastery implied power to defeat the disease and therefore responsibility for its control

Devoting his first lecture to the ætiology of the disease, he said that, when man first appeared, the mosquito was already a well established form of life and had probably already formed its partnership with the protozoon Prehistoric man, at least in some warmer regions, almost certainly suffered from malarial ague, and the disease was to be found in the early historic records of Egypt, India, and China Hippocrates, who described the quotidian, tertian, and quartan fevers, associated the disease with marshy districts he did not spot the intermediary mosquito, but, on the other hand, some physicians today had their eyes so firmly fixed to microscopes that they could not see the significance Hippocrates noted in "airs, waters, and places" The word *malaria* (bad air) was used in Italy during the Middle Ages, by doctors and laymen alike, for the cause of intermittent fevers—not for the illness itself In some parts of Italy the alternative *cattivaria* was used, but *malacqua* (bad water) never had wide currency The miasma from swamps, and even from hill streams, was held responsible for the fever, and as early as the 1st century B C a Roman writer had spoken of the noxious effects of small creatures, invisible to the human eye, which come out of the marshes Various writers were puzzled by the regular rhythm of the fever, which made it clinically unlike an ordinary toxic or inflammatory state and more suggestive of a living multiplying organism Before 1831 Rasori had scored a bull's eye with his account of the behaviour of this hypothetical organism

In the laboratory, examination of the blood showed granules of "malaria pigment," and the malaria parasite was in fact probably seen by Meckel, Delafield, and others In 1876 Joseph Jones, in New Orleans, recognised malarial blood on a stained garment and claimed that by examining the blood he could tell that the patient was in a paroxysm of malaria Laveran made his conclusive observations in 1880, but they were not generally accepted for some years Thus at a meeting in the United States in 1886 Osler expressed grave doubt about Laveran's bodies being the cause of malaria, but he was shaken by the discussion, deferred his Canadian holiday, found the crescentic forms and declared that he had been taught the folly of scepticism based on theoretical considerations

But still nobody knew exactly how natural infection with malaria occurred Over the centuries, the inhabitants of parts of Italy and Africa had associated fevers with mosquitoes and even (as Richard Burton reported in 1856) with their bites Lancisi in 1719 thought that insects from the marshes possibly conveyed to man their own bad humours It was in April, 1894, that Patrick Manson, walking along Oxford Street, told Ronald Ross of his theory that mosquitoes carry malaria parasites just as they carry filariæ This was 14 years after Laveran's discovery, but Ross, working in the tropics, had never seen malaria parasites till Manson showed them to him, for the use of microscopes in the tropics was negligible till this century Ross now went back to India—with a microscope and great zeal, but with little knowledge either of the literature or of the mosquito His observations, and those of Grassi in Italy, provided the conclusive proof And recently, said Dr Russell, the studies of Prof H E Shortt and Prof P C C Garnham at the London School of Hygiene and Tropical Medicine had brought the ætiological story to a climax The malaria parasite could now be followed (but for a few small hiatuses) from the mosquito's beak, through the human body, and back into the insect

The last of Dr Russell's five lectures, entitled Malaria and Society, is being given at the school today, Friday, at 5 30 P M

VIRUSES IN MEDICINE

T[illegible] current issue of the *British Medical Bulletin* deals [illegible]uses in medicine Dr C H Andrewes introduces the [illegible]nd points to the many important advances made in this field by British workers Sir Macfarlane Burnet contributes an article on the ecology of virus diseases, contrasting those which produce life-long immunity with those in which repeated or persisting infections occur Prof Wilson Smith shows how *simple viral immunology* can be, and Dr E W Hurst indicates the difficulties confronting anyone working on the chemotherapy of virus diseases Dr Forrest Fulton complains that in the hierarchy of those who work with viruses it is customary to allot a very humble place to the craftsmen who concern themselves with the minutiæ of technique So the editors of the bulletin cannot be accused of doing so they have rightly given prominence to Dr Fulton's article techniques used in the study of viruses Apart from the general topics, there are articles on specific virus diseases smallpox and related infections (Prof A W Downie and Dr A Macdonald), recent advances in poliomyelitis (A J Rhodes), Coxsackie viruses (Dr J O'H Tobin), the common cold (Dr C H Andrewes), the viruses of epi influenza (Dr A Isaacs), mumps (Prof E T C Spooner yellow fever considered as a problem in epidemiology G W A Dick), infective and serum hepatitis (Dr F O MacCallum), the psittacosis lymphogranuloma group viruses (Prof S P Bedson), Q fever in this country (Dr M G P Stoker), the postinfection encephalitides (Dr E Hurst), and veterinary diseases of medical interest (Dr A Gledhill)

THE MAGNUSON REPORT

Last year the report of the Presidential commission the health needs of the United States was presented by chairman, Dr Paul B Magnuson Vol I, giving the find and recommendations of the commission, was publis last December[1] Volume V has now appeared,[2] and sets the testimony of witnesses at regional public hearings 8 large cities in the United States The narrative is p under the headings of the Consumer of Medical Service Professional Groups, Medical Care, its Provision and Payment, Professional Education, Health Problems Va and Rebuilding Health and Usefulness There are also of witnesses, case histories, and a useful index

DEFECTIVE OR DEAF

Many children who are born deaf or become deaf at early age—and especially if they develop emotional dis ances as a result—are certified as mentally defective remain in institutions for the rest of their lives. Dr Minski, whose annual report from Belmont Hospital attention to their fate, describes a small unit which he has up for the study of such children

The unit has been financed for a year by the South-Metropolitan Regional Board, from their research funds, King Edward's Hospital Fund for London have given a towards the equipment—including such things as audio gramophones, and headphones The unit opened last M taking six children Miss Edith Whetnall, who besides an aural surgeon is an authority on deafness, is taking in the work, and Dr Minski supervises the clinic from psychiatric point of view The team includes, besides electro encephalographer, a psychologist, a teacher of the deaf, a mentally trained nurse, and four children's visors, and it also has the help of the occupational ther

Such misdiagnosed children, being unable to speak, give picture very like mental defect Yet if their disability been diagnosed early they would have responded to training in schools for the deaf, and have been able to live normal lives In the unit, the six chosen patients are studied psychologically and also by encephalography, psychogalvano and audiometry Their response to teaching and supervision is also recorded The aim is to devise tests which will distinguish the mentally defective from the deaf, which also, no doubt, will measure the degree of defect in those who have both disabilities This, of course, take some time, but meanwhile the team have been encouraged to find that the brightest child in the group, a boy who has already spent six years in an institution for defectives, is merely deaf and not mentally defective at A practical problem is that a child like this needs inte education, to help him to make up his leeway, before he ble to benefit from the teaching in an ordinary school for the eaf Dr Minski suggests that a special school is needed for uch children, where they can be given more individual and ntensive training than is possible in a school for the deaf The regional board are approaching the Ministries of Health nd Education about the possibility of providing such a school ertainly children so unnecessarily handicapped need some pecial consideration and help

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[1] *Lancet* 1953, i 388

[2] Building America's Health a report to the President by President's Commission on the Health Needs of the N Vol V The People Speak—Excerpts from Regional Hearings on Health Pp 521 U.S Government Office Washington

NEW MEDICOLEGAL JOURNAL

The *Journal of Forensic Medicine*[1] a new quarterly ponsored by the Medico Legal Society of Johannesburg nd edited by Dr H. A Shapiro is intended to serve an nternational need by providing space for papers on those iverse and apparently unrelated *fields of scientific inquiry* which together constitute forensic medicine An editorial in he first number suggests that the present dispersal of papers n this subject is undesirable and interferes with their ready ppraisal by those who can appreciate their medicolegal ignificance

The first number comprises eight papers K M Bowden, of Melbourne writing on Sudden or Unexpected Deaths in nfancy analyses 320 such cases, 216 of which were of patients nder the age of one Acute infection of the respiratory tract common cause of death may be readily overlooked if the ung parenchyma is the only portion selected for histological tudy for disease may be confined in early cases to the larger ronchi Acute epiglottitis or acute laryngitis may be respon ible for extremely rapid death from intense inflammatory welling In 27 cases (8·4% of the total) a non-specific acute yocarditis was found ; this might have been overlooked had ot the tissue been examined histologically Widespread yocarditis was found in one baby who died on the first ay of life so it was concluded that the disease had been resent in utero Two episodes of acute non-specific myo arditis were observed in Melbourne—the first in 1949–50 t the time of an outbreak of poliomyelitis and the other n 1952. This disorder has also been found in association ith inflammatory changes in the meninges (meningomyo arditis) and with inflammatory changes in the upper part of he respiratory tract

Lester Adelson of Cleveland Ohio discusses Possible eurological Mechanisms Responsible for Sudden Death hile there are valuable papers on the Estimation of Stature rom the Long Bones by E N Keen, of Cape Town and h the Estimation of Age from Cranial Sutures by Ronald nger of Cape Town L. Prinsloo of Durban reports how the eletal remains were successfully identified in the Howick alls Murder Case while E O K Harwood, of Pretoria ows how circumstantial yet completely damning evidence s obtained in a case of murder by identification of a nture.

This journal will surely be welcomed by forensic patho ists, and possibly also by authors and readers of crime tion.

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niversity of Cambridge

Dr Sven Moeschlin of the University Medical Clinic rich, will deliver a lecture on Friday Nov 20 at 4.30 P.M. the Department of Pathology Tennis Court Road He to speak on Immunological Aspects of Agranulocytosis.

On Oct 17 the degrees of M B., B CHIR. were conferred on O K Parsons.

niversity of Leeds

Dr Andrew Bogdan has been appointed senior registrar d tutor in pædiatrics ; and Dr I Bruce has been appointed urer in the department of anæsthetics.

ersity of Glasgow

T J Honeyman F.R.F.P.S., director of Glasgow Art lleries, has been elected rector of the university Dr neyman graduated M B at the university in 1916 and tised medicine until 1929

yal College of Physicians of London

Prof E J Wayne will deliver the Bradshaw lecture on rsday, Nov 12, at 5 P.M., at the college Pall Mall East ndon S W 1 He is to speak on the Diagnosis of Thyro icosis.

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[1] Published by Juta & Co Ltd., P O Box 30 Cape Town 42s. per annum ; 12s. 6d per copy

Royal College of Surgeons of Edinburgh

At a meeting of the college held on Oct 21 with Prof Walter Mercer the president in the chair the following were admitted to the fellowship

Festus Olaniyi Adewole Maqbool Ahmad Derk Crichton A B McL. Currie, Eli Davidowitz, K. R. Daymond, L. P Eaton, Fazal Elahi, J M. Foreman Toufic Elias Haddad Shaikh Abdul Hamid J M. Hastings Harry Koo Herman Klein Polavaram Lakshmipathy William Markkanen, Mithlesh Kumar Mehra, Nurgesh Darashaw Motashaw Hugh H Neifeld Kamal Mohamed Said Ganga Prasad Srivastava, N L. Stokoe, E. R. Treasure Mohsin Ali Vali G S Watson, J B R. Wells A. O Wilson C G Wilson, Abdullatif Ibrahim Yashruti.

Royal College of Physicians of Ireland

At the annual meeting of the college on Oct 19 Dr Edward T Freeman was elected president and Dr J A. Wallace vice-president

Royal Society of Medicine

On Oct 20 the gold medal of the society was presented to Sir Gordon Holmes F.R.S

Alfred Adler Medical Society

At a meeting at 8 P.M. on Thursday, Nov 12, at 11 Chandos Street London W 1 Dr T F Cotton will speak on the Psychological Element in Cardiac Disease

Research Defence Society

Sir James Learmonth will deliver the Stephen Paget lecture at a meeting of this society at University College, Gower Street London W C 1 on Thursday Nov 19 at 5.30 P.M. *He will speak on the Surgeon s Debt to Animal* Experiment

Institute of Dermatology

The institute is holding a series of semipermanent exhibitions during the winter course in conjunction with the department of medical illustration of the Hospital for Sick Children The second of the series is by Dr J A. Dudgeon on Virus Diseases of the Skin, and will be held from Nov 2 to 24

Royal Society

Mr Kenneth M Smith, F.R.S. will deliver the Leeuwenhoek lecture at the society Burlington House Piccadilly London W 1 on Thursday, Nov 5 He will speak on the Behaviour of Certain Viruses in their Hosts and of their Development in the Cell On Thursday Dec 10 Sir Francis Walshe, F R.S., will deliver the Ferrier lecture on the Contribution of Clinical Observation to Cerebral Physiology Both lectures are at 4 30 P M

College of General Practitioners

The first annual general meeting will be held on Saturday Nov 14, at 2 P M., in the great hall of B.M.A House, Tavistock Square, London W C 1 Foundation membership and asso ciateship will close on that day

The agenda for this meeting and the first annual report of the college were despatched to all members and associates on Oct 23 Any member or associate who has not received them is asked to communicate with the Secretary at 14 Black Friars Lane E C.4

Increased Number of School Dentists

There are now more dentists in the school dental service than there were before the introduction of the National Health Service in July 1948 Miss Florence Horsbrugh, the Minister of Education speaking at the annual dinner of the Society of Medical Officers of Health in London on Oct 22 said that by January 1948 the number of dentists in the school dental service had risen to the equivalent of 921 full time dentists but by January 1952, it had fallen again to 713. Today the figure was 928 This was an encouraging improvement but she wanted a larger school dental service and the Education Act 1953 had made clear to local education authorities their duty to provide such a service with comprehensive facilities for treatment

Leeds Old Students Dinner

The annual dinner of past and *present men students of the* School of Medicine of the University of Leeds will be held at the Hotel Metropole, Leeds, on Friday Nov 27 at 7 30 P.M when Sir Henry Cohen will be the guest of honour Tickets may be had from the hon secretary D A Youdale the Medical School Leeds, 2.

Royal Sanitary Institute

At a meeting of this institute to be held at Dudley Town Hall on Friday, Nov 27, at 10 15 A M, Dr Hugh Paul will speak on Infectious Disease—the New Look

Foot Health

This subject has been chosen for the annual seminar of the Central Council for Health Education for 1954 The seminar will be held at St John House, Collingham Gardens London, S W 5, from Feb 23 to 27 The programme will include a lecture by Mr T. T Stamm on Foot Function Further particulars may be had from the secretary of the council, Tavistock House, Tavistock Square, W C 1

Christian Medical Fellowship

At a meeting of this fellowship to be held at B.M A House, Tavistock Square, London, W C 1, on Monday, Nov 2, at 7 45 P M, Dr Robert Cochrane will open a discussion on Leprosy and its Challenge to Christianity

The fellowship is also holding a house party at Rustington Hotel, Sussex, from Nov 20 to 23 The main theme will be Is It My Concern ?—a Consideration of the Christian in Medical Practice The speakers will include Dr Margaret Edmunds, Mr Gerald Golden, Dr T S Goodwin, Dr J D Griffiths, Dr H Julyan Hoyte, and Dr W B Young Further particulars may be had from Mr L A H Snowball, Wakefield House, Compton Street, Eastbourne

The British Pharmacopœia 1953

On Wednesday, Nov 4 at 7 30 P.M, at the house of the Pharmaceutical Society of Great Britain, 17, Bloomsbury Square, London, W C 1, Mr T C Denston, PH C secretary of the British Pharmacopœia Commission, will give the first of a series of five lectures on the new *Pharmacopœia.* Other speakers will be Prof W H. Linnell, D.SC (Nov 12), Prof H Berry, F R I C (Nov 18), Prof A. D Macdonald, M.D (Dec 2), and Dr A A Miles, F R C P (Dec 10)

Commission on Divine Healing

The Archbishops of Canterbury and York have appointed a commission on divine healing[1] It will consider the theological, medical, psychological, and pastoral aspects of divine healing, and it will aim to provide a report which will guide the Church to a clearer understanding of the subject, which will help the clergy in the exercise of the ministry of healing and which will encourage increasing understanding and coöperation between them and the medical profession. The medical members of the commission are Dr J A Hadfield Dr Ronald Henson Dr Ronald Cove Smith, Prof. A Moncrieff, Sir James Paterson Ross, Dr Denis Brinton, and Dr David Stafford Clark Communications should be addressed to the secretary, Lambeth Palace, London, S.E.1

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[1] *Times* Oct. 21, 1953

Diary of the Week

NOV 1 TO 7

Monday, 2nd

Postgraduate Medical School of London, Ducane Road, W 12
4 P.M Dr William Evans Electrocardiogram in Cardiac Pain.
Royal Eye Hospital, St. George's Circus S E 1
5 30 P M Miss J M. Dollar Management of Diseases of Uveal Tract.

Tuesday, 3rd

Royal College of Surgeons, Lincoln's Inn Fields W C 2
5 P M. Mr H A Haxton Sympathetic Supply of Upper Limb (Arris and Gale lecture)
British Postgraduate Medical Federation
5 30 P M (London School of Hygiene and Tropical Medicine, Keppel Street, W C 1) Prof E J King, PH D Alkaline and Acid Phosphatases
Royal Society of Medicine, 1, Wimpole Street, W 1
8 30 P M *Section of Orthopædics* Dr R. O Murray Cystic Tuberculosis of Bone Mr P Jackson Treatment of Opposition Paralysis of Thumb Mr B J S Grogono Injuries of Atlas and Axis.
Institute of Dermatology St. John's Hospital Lisle Street, W C.2
5 30 P M Dr J A Dudgeon Viral Diseases of Skin
West End Hospital for Nervous Diseases, 40, Marylebone Lane W 1
5 30 P.M Mr Colin Edwards Neurological demonstration

Wednesday, 4th

Society of Apothecaries of London, Black Friars Lane Queen Victoria Street, E C 4
4 P M Dr J B Harman Management of Inoperable Malignant Disease
5 15 P M Dr F Lee Lander Asthma and its Treatment.
Postgraduate Medical School of London
2 P.M Dr F V Flynn Na and K Metabolism
Royal Society of Medicine
5 15 P M *Section of History of Medicine* Prof Ludwig Edelstein History of Greek Medical Empiricism Sir Zachary Cope Great Windmill School of Anatomy
8 P.M *Section of Surgery* Dr J F Nuboer (Utrecht) Mr Philip Allison Carcinoma of Cardiac End of Stomach
Royal Institute of Public Health and Hygiene 28 Portland Place, W 1
3 30 P M. Lord Amulree Geriatrics
Institute of Dermatology
5 30 P M Dr Dudgeon Viral Diseases of Skin
Institute of Urology, 10 Henrietta Street, W C 2
5 P M Mr A R. C Higham Enuresis
Midland Medical Society
8 15 P M. (Birmingham Medical Institute 154 Great Charles Street Birmingham, 3) Dr J C Gilson Is Coal-dust Harmful to Man ?
Manchester Medical Society
4 30 P M (Medical School University of Manchester) *Section of Medicine.* Dr Denis Williams Inquiries into Cerebral Basis of Temperament and Personality
Medico Chirurgical Society of Edinburgh
8 30 P M (Royal College of Surgeons 18 Nicolson Street Edinburgh) Dr A Stewart Henderson Dr R. E Verney Problems of Student Health (Joint meeting with Royal Medico Chirurgical Society of Glasgow)

Thursday, 5th

College of General Practitioners
5 45 P M. (14 Black Friars Lane, E C 4) Dr Geoffrey Barber Common Ailments met in General Practice and Seldom Seen in Hospitals
University of London
5 P M (1 Wimpole Street, W 1) Prof F C Ormerod Management of Cancer of Larynx (Semon lecture.)
Royal Medico Psychological Association
2 15 P M (1, Wimpole Street, W 1) Earl Jowitt Medicine and the Law (Maudsley lecture)
British Postgraduate Medical Federation
5 30 P M (London School of Hygiene and Tropical Medicine) Dr P M F Bishop Physiological Action of Sex Hormones
Institute of Child Health and Institute of Neurology
5 30 P.M (National Hospital, Queen Square, W C.1) Dr E A Carmichael Hemiplegia
Institute of Obstetrics and Gynæcology
3 30 P M (Queen Charlotte's Hospital Goldhawk Road, W.6) Prof A A Claye Forceps in Present-day Practice

Friday, 6th

Postgraduate Medical School of London
4 P.M Prof. Melville Arnott Peripheral Vascular Disease
Royal Society of Medicine
10 30 A.M *Section of Otology* Mr R. R. Simpson History of British Otology (Presidential address.)
2 30 P M *Section of Laryngology* Mr C P Wilson Lateral Cysts and Fistulæ of the Neck. (Presidential address.)
5 30 P M *Section of Anæsthetics* Prof R. R Macintosh Anæsthetist Abroad (Presidential address.)
Royal Eye Hospital
4 30 P.M Mr A J Cameron Recent Advances in R Detachment Surgery
Institute of Dermatology
5 30 P M Dr Brian Russell Pyogenic Infections.

Saturday, 7th

Institute of Laryngology and Otology, 330, Gray's Inn Road W C 1
11 30 A.M. Prof E Luscher (Basle) Psychical Factors in Nose and Throat Diseases
Institute of Obstetrics and Gynæcology
NOON (Hammersmith Hospital Ducane Road W 12) Stallworthy Genital Tuberculosis

Appointments

Hellings, Pamela M.B Brist, D.A anæsthetic registrar Norwich Hospitals
Hulme Allan B A M B Camb, F.R.C.S consultant neurosurgeon to the South Western Regional Hospital Board in the department of neurosurgery, Frenchay Hospital Bristol.
Sutherland I B M B Edin, D P H, asst. M O.H., County Councils of Roxburgh and Selkirk.
Wilson H L J M A M B Camb, F.F A, D.A, part time consultant in anæsthetics, United Sheffield Hospitals.

Births, Marriages, and Deaths

BIRTHS

Fisher —On Oct. 22, at the Royal Maternity Hospital, Belfast, to Sheila wife of Oliver D Fisher, M D M.R.C.P—a daughter (Amanda Jane)
Solomons —On Oct 2 in Dublin, to Joan (née Maitland), wife of Michael Solomons M R.C O G —a son

DEATHS

Shepherd —On Oct. 19 at 27, Sea Lane Goring-by-Sea, Robert Chaplin Shepherd M B Lond, M R C P

OBJECTIVE EXAMINATION PAPERS IN THE MEDICAL CURRICULUM

D C SINCLAIR
M.A. Oxfd M.D St And
UNIVERSITY DEMONSTRATOR IN HUMAN ANATOMY
UNIVERSITY OF OXFORD

MOST medical students regard examinations with most painful concern and indeed the influence which ey wield for good or ill renders them worthy of respect raminers however often make less effort than they ould to think critically about the too familiar weapons ey use, and in Britain medical examinations follow a irly stereotyped pattern It is therefore stimulating observe the objective type examinations of the edical schools of the United States, and to try to assess eir value in relation to the more conservative methods far used by British schools This article is not con rned with arguments as to whether or not examinations any type are desirable phenomena it merely accepts e situation that the vast majority of medical schools roughout the world employ them

The Traditional Examination Paper

FORMAT

In Britain written papers are usually three hours long d the student has to answer some five or six questions ; is usually allowed a restricted choice by the inclusion one more question than he needs to answer He has us a considerable time for each of the questions which so framed that he has to treat the subject at moderate igth. Questions are usually of the essay ' type roduced by the words ' Discuss,' Describe, ' " Give account of ' ' Compare and contrast," and the like, ly occasionally varied by ' Write short notes on,' or, rely ' Tabulate.

This format imposes fairly narrow specifications on h question : it must be capable of being answered in time provided yet must not be too short it must t be too difficult nor yet too easy it must be com tely unambiguous (the examination hall is full of sea yers) and it should be capable of connected and lerly treatment. It is a difficult task to frame a isfactory question meeting all these requirements ich has not, in one form or another been asked before. nce the frequency of old favourites, well tried questions ich have already served to distinguish the sheep from goats.

ASSESSMENT

For all professional examinations in Britain it is usual have at least two examiners and this arrangement tects the student against having his future decided on basis of one opinion only It can operate in this way ly if both examiners read all the scripts or if some er safeguard is adopted The assessment of (and netimes the mere physical act of reading) the average ay type of script is a time-consuming affair and it is en impracticable for both examiners to read every ipt. A common compromise is to mark by questions her than by candidates each examiner marking f the questions.

Many systems of assessment are in use (Vernon 1940) first sight it seems only necessary to establish whether candidate ought to pass or to fail but the paper ely forms the whole of the examination, and the essment of the script has to be made in conjunction h the oral and practical examinations. For this son a simple pass or fail system is not sufficient and e sort of scale is necessary so that the result can be en due weight

The most familiar method is to grade scripts in per centages drawing an arbitrary line at the pass level which is usually 50% Such scoring is a mere arithmetical convention a percentage of an abstraction. In medical subjects the examiner cannot sit down with a calculating machine and a list of all the possible points which could be made he records merely an impression having con stantly in mind the pass mark Nevertheless, so used are we in our daily life to handle figures which have been derived by legitimate mathematical means that he may be deluded into thinking he is performing an arithmetical operation, instead of using an arithmetical notation to record a fairly gross subjective judgment Just how much these subjective impressions and the marks which reflect them can vary has been shown by experiment with rather frightening results

For example Hartog et al (1936) obtained fifteen scripts which had all received the same moderate mark in a School Certificate examination in history, and circulated them to fifteen experienced examiners each of whom marked the scripts and placed the candidates in the category of ' fail ' pass,' or ' credit Over twelve months later the same scripts were resubmitted to the same examiners for the same procedure to be gone through On the first occasion the marks ranged from 21 to 70 out of 96, and on the second from 16 to 71 The difference between the highest and the lowest marks allotted to one of the candidates was 30 marks In 92 instances the examiners altered their original verdict of ' fail, ' pass, or " credit at the second time of examination and one examiner changed his mind about eight of the fifteen scripts he examined. In another part of the same investigation one candidate in School Certificate English was awarded marks varying from 28 to 80 out of 100 by seven different examiners.

Similar results have been obtained by other workers (Vernon 1940) and though no studies appear to have been made in medical subjects, there seems no reason to suppose that they would constitute an exception.

COMMENT

The essay type of examination is used to discriminate between students perhaps more often than any other educational test We should therefore ask ourselves what qualities and achievements it evaluates. This is not a simple question to answer but it is possible to make a rough list.

The essay type examination tests the ability of the candidate to comprehend simple written instructions at a moment of stress and, having done so to apportion his limited time judiciously It tests his factual recall and his power to select the most important relevant facts of which he is master It tests the speed and precision with which he can arrange and set down these facts in logical order and his capacity to develop with them a reasoned argument or a concise description It tests his ability to write spell, and punctuate his own language legibly and fast, his capacity to use and understand the language of science, his neatness and tidiness and finally the ingenuity with which he can conceal his own ignorance

Now many of these skills are undoubtedly desirable in a doctor as, indeed they are in any educated man

Intelligence is not listed among them since the results of essay type examinations do not correlate well with the scores obtained by candidates in tests which are commonly held to measure intelligence (Edholm and Gibson 1944 Bartlett 1953) It ought, perhaps, to be stressed that factual recall is only one among many achievements tested, and is placed in a wide setting concerned with the use of factual knowledge The way in which a candidate sets about answering a question is often just as big a factor in his success as the battery of facts he can unmask

On the other hand, the limited number of essay-type questions it is possible to ask in a single examination means that the sample taken of the student's knowledge will be small, unless the questions themselves are broad and comprehensive All examinees know that this is not always so, and questions which demand a detailed knowledge of a restricted field lead the student to cram his mind with detail to the detriment of his grasp of the broad outlines of the subject From this type of question also derives the time honoured practice of "spotting" questions, so that small sections of the subject are worked over to the exclusion of others because they are "bound to come up again this time"

The testing "in depth" of a limited part of the student's comprehension of the subject thus leads to an undesirable element of luck in the examination, and the student also feels that his future depends on an arbitrary selection of questions A single paper of six questions thus becomes a formidable psychological obstacle, causing students to work for the examination only, and not to attempt to acquire a grasp of the subject for its own sake For this reason it is often suggested that a second paper should always be given, to spread the load more evenly This argument is, however, capable of infinite extension, and the ground covered by two papers, though admittedly twice that covered by one, is still a small fraction of the whole subject

But the commonest objection to the essay-type paper is the extent to which the candidate is dependent on the examiner's purely subjective judgment Though discrepancies are smoothed out by compromise between the examiners, and also by the candidate's performance in the oral examination (if given), an uneasy feeling must remain that an educational test where such variability in assessment is possible is not wholly satisfactory

It is considerations of this kind, allied to the impracticability of marking vast numbers of essay-type scripts in a limited time, that have led to the introduction of the objective examination into medical subjects

The Objective Examination Paper

HISTORY

The objective examination has a history extending back some forty years, and is now a commonplace in American education up to, and often including, the college level In this country its influence has not yet extended much beyond the "eleven-plus" examinations The idea is that more of a subject can be covered by asking a large number of short questions rather than a few long ones, and that the questions can be put in a form that leaves marking independent of the examiner's subjective judgment It has been possible to eliminate altogether the human element in the marking process since 1937, when the International Business Machines Corporation developed a machine which would mark test papers electrically This has led to the widespread use of objective tests for many purposes throughout the United States, and some American universities now have a special objective examination service, which administers all university examinations

The introduction of this type of test to the medical curriculum is relatively recent, but in 1950–51 the National Board of Medical Examiners in the United States successfully converted their examinations in pharmacology and internal medicine to the objective format As a result, the Board is adopting similar measures for all the examinations under its control This step is being taken with the assistance of the Educational Testing Service, an organisation which specialises in the design, handling, and assessment of many similar tests, ranging from the United States Military Academy entrance examinations to the Medical Colleges Admission Test, which is now insisted upon by the majority of A medical schools (Stalnaker 1950) Such a move by the National Board, which is the only examining body recognised by virtually all the States in the Union, is bound to have a great influence on the type of internal examinations set in individual medical schools.

MULTIPLE CHOICE EXAMINATION

The National Board of Medical Examiners (195 publish a small booklet which gives examples of the ki of question the student may expect They are all of multiple choice type, in which the student is presen with a question and five possible answers, his duty merely to indicate his choice of the best of these answ There are usually 200–300 of these questions to answered in an examination lasting three hours but exact number varies with the subject The stud indicates his choice by blackening a labelled space in special answer sheet with a soft pencil, no writing involved

The questions are usually arranged in groups, group falling under a specific set of instructions. It not practicable to give examples of all types of ques but a few of the possibilities may suffice to indicate scope of the method as applied to medical subj they are all taken from the National Board's booklet

The simplest type is as follows

Directions—Each of the following questions or incom statements is followed by five suggested answers or pletions Select the one which is best in each case and bl the corresponding space on the answer sheet

Q In airborne first-infection tuberculosis the prim focus is most commonly found in the

(A) periphery of the lung
(B) tonsil
(C) apex of the lung
(D) tracheobronchial lymph nodes
(E) hilus of the lung

There are many variants of this

Directions—Each group of questions below consists of lettered headings followed by a list of numbered words phrases For each numbered word or phrase select the heading which is most closely related to it and blacken corresponding space on the answer sheet

(A) Quinidine
(B) Theophylline
(C) Amyl nitrite
(D) Glyceryl trinitrate
(E) Papaverine

Q Increases the contractile force of the heart and diuretic

Another type of question requires quanti information

Directions—The following paired statements describe entities which are to be compared in a quantitative On the answer sheet blacken the space under

A if (A) is *greater than* (B)
B if (B) is *greater than* (A)
C if the two are *equal or very nearly equal*

Q (A) The amount of glycogen in the cells of Henle's in a diabetic

(B) The amount of glycogen in the cells of Henle's in a non diabetic

The directions may be quite complicated

Directions—Each of the following pairs of phrases desc conditions or quantities which may or may not be On the answer sheet blacken the space under

A if increase in the first is accompanied by increase in second or if decrease in the first is accompanied by de in the second,

B if increase in the first is accompanied by decrease in second or if decrease in the first is accompanied by inc in the second,

C if the second remains constant, or approx constant, when the first increases or decreases.

Q 1 Cerebrospinal fluid pressure 2 Intra-ocular p

In the preceding group of questions only possibilities are presented to the candidate, but in a similar group there are five

Directions—Each of the following sentences consists of two ain parts; a statement and a reason for that statement. n the answer sheet blacken the space under

A if the statement and the proposed reason are *both true* and are *related* as cause and effect;

B if the statement and the proposed reason are *both true* but are *not related* as cause and effect;

C if the statement is *true* but the proposed reason is *false*;

D if the statement is *false* but the proposed reason is *an accepted fact or principle*;

E if the statement and the proposed reason are *both false*

Q The corpus luteum of menstruation becomes the corpus iteum of pregnancy because progesterone inhibits the activity f the anterior portion of the pituitary gland

Another group of questions consists of several case-istories, each followed by a series of questions each with ve possible answers these questions deal with such atters as the most likely diagnosis, the most likely dditional physical finding the probable outcome of the isease if left untreated, and so on

Setting the questions is a laborious task, for on their xact form a great deal depends. The procedure in tting the National Board examinations is outlined by ie Educational Testing Service in their booklet *Building Test* (1953) The questions in a particular subject are cided at a meeting of the examiners and cast into a itable form with the help of a member of the testing rvice. After checking the questions are experimentally dministered to a group of students, usually by including iem as unscored items in another test on the same ibject The answer sheets relating to these items are en subjected to a process known as 'item analysis,' hich shows how many students selected the 'keyed' correct answer and how many selected each of the decoys A good question is one which good students s evaluated by their score on the whole test) will answer rrectly more often than mediocre or poor students and is possible to give mathematical expression to the pacity of the question to discriminate between good id bad students.

The results of item analysis often lead to recasting the question For example, if it is found that good idents tend to prefer one of the 'decoys' instead of e 'keyed' answer, the wording is immediately spect. Indeed, the wording is often extremely impor nt. If one of the decoys is several words longer than e others, this in itself will attract more preferences from or students. Two of the decoys may overlap so that one were correct the other would have to be also or nversely they may be self-exclusive so that if one is rrect one or more of the others cannot be Pure logic ay thus lead a candidate to the correct answer (Vernon nd Davis 1950)

The questions on trial are also rated for difficulty the n being to provide in the final assembly of questions a ge from items that are easy to those which are tremely difficult so that the average student will swer slightly more than half the items correctly (In is type of examination the pass mark is just as arbitrary in essay questions; the students are ranked in order their prowess in the examination and a subjective cision has then to be taken as to where the failure-line st be drawn) The speed with which the questions n be answered is also taken into account and adjust nts are made so that 80–90% of an average class have ne to attempt all the questions in the final assembly hen the test is put together it is again checked, and ven to another batch of students for final trial

All questions are regularly reviewed by the committee examiners, and so kept up to date in the light of reasing knowledge Medical questions are perhaps ticularly difficult to frame for as the National Board Medical Examiners point out:

> in the broad field of medicine contrast may not be rply defined as between black and white but rather varying shades of grey In answering these questions, therefore, one should look for the best choice, and not be misled by other choices which might be considered possible but still less applicable than the one considered correct In each case the test committee has agreed that there is only one best answer

It is often hard to find a sufficient number of decoys which will really decoy If one or more of them is too obviously unacceptable, the choice is no longer between five answers, but between a smaller number with a correspondingly greater random chance of hitting the correct one.

The process of setting an objective type examination containing perhaps 200 questions is thus not to be undertaken lightly and expert advice is not available in every medical school Many amateurs may find hard wrought questions ruined by the curse of unsuspected ambiguity which sits on the shoulders of everyone who has put inquisitorial pen to paper Nevertheless these examiners reap their reward when the time comes for assessing the answer sheet.

Under the objective system the booklet containing the questions is handed in again at the end of the examination and can be used a second time at some future date It is possible in this way to accumulate a stock of questions of such magnitude that after the initial labour the examiner will never need to set any more but will simply draw a fresh combination of questions from his stock. His duties as an examiner would then reduce to servicing his questions and assessing the results, which if a machine is available is almost an automatic process The general opinion is that a stock of some 5000 questions in a given subject would ensure an examiner a life of ease and comfort, but the student fraternities are attempting to circumvent such proposals by industriously setting their members the duty of memorising two or three questions each and writing them down after the examination for future study Most examiners however feel that it is more difficult for a student to memorise the answers to 5000 questions than it is for him to learn the subject

ASSESSMENT OF MULTIPLE CHOICE EXAMINATIONS

If the tests are hand scored the rate of correction may be up to 50 answer-sheets an hour If electrical marking is used the answer-sheet is inserted in a special machine in which a large number of electrical contacts are masked by a master stencil with holes cut in it corresponding to the position of the correct answers in the test being marked. The pencil marks allow a current to flow through the contacts and the machine counts the number of correct and incorrect answers by measuring the amount of current flowing The score may be read off directly from a meter, and the machine will also register percentages part-scores, right answers minus wrong answers (or any desired fraction of wrong answers) and so on at will. The operator has thus merely to insert the sheets and write down the scores, so that it is possible to score 700–800 tests an hour I understand that a further development of the machine is proposed in which the mark obtained will automatically be printed on the answer-sheet It is a sad commentary on human frailty that it is often necessary to go over the answer sheets before scoring to ensure that the pencil marks are adequately black.

Machines enable an immense amount of data to be analysed quickly and since the scoring is truly arithmetical, statistical comparisons are valid It is possible to compare directly the performance of two groups of students or the performance of the same group on different sections of the test Thus, if the students of a particular medical school equal or surpass the mean performance of those in all other medical schools in every subject but one it is pertinent for the school to inquire into the teaching of that subject. It is also interesting that on at least one occasion an analysis of the machine-marked results has revealed a leakage of information about the content of the examination (Cowles 1953)

OTHER TYPES OF OBJECTIVE QUESTION

Though the multiple choice question is generally regarded as the most useful and reliable, many other objective questions are in use

(*a*) *True or false* —This is the simplest form of multiple choice, and has similar advantages and defects, but the element of chance is greater An example from a recent histology paper reads

Directions —Encircle the appropriate letter to indicate each statement as either true or false

Q T F Blood vascular channels are present within lymph-nodes

(*b*) *Matching* —The candidate has to match a set of items with their attributes This is sometimes done in tabular form—e g ,

Directions —Indicate which of the cells or tissue elements listed below are normal components of the organs which head each of the following columns Place an X mark in the appropriate square

(There follows a list of ten tissue elements ranged down one side of a square along the top of which are arranged ten organs)

(*c*) *One-word and "fill-in"*—These have to be answered by one word or one phrase only—e g ,

Q In what organ is the sequence arteriole–capillary–sinusoid–venule found ?

Fill-in questions may leave several blank spaces in a sentence

Q The presence of.............. ....and..................tissue in the tunica..................of arteries enables them to accommodate fluctuations in blood pressure and volume, while the presence of ....in the tunica..................prevents over distension.

(*d*) *Various* —Considerable enterprise is being used in framing new variants of the objective pattern Duplicated diagrams or drawings are left with the leaders unlabelled, and the student has to fill them in , he may have to complete tables showing the contrast between two diseases or drugs, to recognise structural chemical formulæ, to give a one-word diagnosis or a one-word treatment on the basis of brief case-histories, and so on The department of psychiatry at Johns Hopkins use a test in which eight brief biographical sketches are separated into two parts (1) the later career , and (2) the early life and family background The student has to fit them together

COMMENT

The objective paper clearly allows a more extensive sample to be taken of the student's knowledge, though the sample in different areas may penetrate to varying depths beneath the surface In comparison with the essay-type examination, the skills tested are not so numerous Chief among them are the ability to comprehend written instructions and the power of discrimination, the ability to reason from cause to effect is also tested in certain questions Almost of necessity, the questions aim at the uncovering of factual knowledge, but the power of factual recall is not so heavily drawn upon as in the essay question In multiple choice questions, the student has at least the advantage of knowing that the fact he is required to remember is in front of his nose, if he can but chip it out from its matrix of irrelevancies The element of guesswork is constantly present (Ruch 1929), and the student who answers completely at random will score marks through ignorance (For this reason it is common to weight the marks in such a way that wrong answers are taken into account as well as right ones) There is no opportunity for originality in the answer, and the student cannot be asked his views on any debatable point The candidate's powers of self-
n and his ability to expound a logical argument or a methodical description are not tested, nor is his
in spelling and writing his own language grammatic

The form of the multiple choice question is
to the form of certain questions asked in intellige
tests, and it might be expected that "intelligence" wo
be considerably involved in objective examinations
this sort, though direct evidence of this for me
students does not seem to be available

Subjectivity has by no means been eliminated
objective type examinations , it has merely been tr
ferred from the marking of the questions to the se
of the questions Individual examiners may set ques
of widely differing standard, and have their own view
the best answer Thus Pullias (1937) found a relati
low correlation between the marks of the same stud
in objective examinations designed to cover the
subject but set by different examiners This obje
is, however, largely met by having the questions
by a large committee of examiners

Again, the determination of success or failure is
an arbitrary decision The failure level must be de
mined after the marks are known and not before, and
thus related to the mean performance of the whole
and not to any absolute value This is known as "
on the curve," and in effect converts the exam
into a competitive one

Cowles and Hubbard (1952) obtained evidence
favour of the multiple choice examination during
trial change over of the National Board of M
Examiners' examinations in pharmacology and in
medicine In each subject, two hours were give
essay type questions and one and a half hours to mu
choice questions The medical schools furnished
fidential reports stating which students in their op
were in the top 20% of the class and which were in
bottom 20% It was found that in both subjects
correlation of objective test scores and medical
ratings was significantly higher than the correlat
essay scores and school ratings, and Cowles and Hu
consider that

> "(1) the objective examination, when carefully
> diligently prepared, appears to offer more reliable and
> evaluation of the student's knowledge and his ability to
> that knowledge to the situation in hand than can be o
> from the time honoured essay examination , (2) the ob
> examination lends itself to thorough statistical analys
> that it may be accurately and intensively assessed, leadi
> recurrent revisions permitting steady improvement of
> examinations "

Nevertheless, many people, both in the United
and elsewhere, watch the advance of the ob
examination with concern, because they feel that
examinations test only a limited number of the qu
which are needed by a doctor Already in some Am
medical schools there are students who have never
exposed to any other form of examination thro
their whole educational career It is felt that
students should at least have the opportunity of
ing their opinions on paper Many schools, th
while including multiple choice questions in their in
examinations, continue to ask other types of questi
well In some instances these are full blown
questions of the traditional type, but in other
attempt has been made to avoid some of the draw
of the essay question, usually by means of short-a
questions

Short-answer Questions

Here a restricted space is provided for the stu
views, and he has to achieve a compression of his
which must therefore be stripped of the unn
verbiage so common in essay-type answers (Dobbie
Barnes 1950) The key-words in such questions
"Define," "Outline," "Name," and so on—e g ,

Q Define adequately in one well constructed sentence any ur of the following : (limit $1^1/_2$ pages)

1 sarcoplasm
2 reticulum
3 serosa
4. parenchyma
5 arteriole

Q Outline under well planned headings and subheadings otal of 20–25) a discussion of ‘ The human skin and its erivatives.

uch questions test the student's grasp of essentials and npose little strain on the examiner they may, in fact e termed ‘ semi objective.”

General Discussion

All medical examinations basically seek to establish hether the student has a command of the subject dequate for him to be considered fit to undertake the ractice of medicine, either immediately or at a later date Roberts 1946) It is in this sense of an achievement est that examinations are usually regarded. Yet they ave a value as a teaching medium for students if the aper is discussed with the class after it is over and ome schools give out model answers for this purpose hey can also teach those teachers who take the trouble find out from the results which parts of the subject ave not penetrated their students' understanding ernon 1940)

The essay type examination is still the standard strument for distinguishing between good and bad udents Such papers are the means by which success failure are often determined scholarships won and mours awarded. They have on the whole, worked uitably in the past, and may continue to do so in the ture. Yet some people have the knack of answering say questions, and others though equally capable udents, have not Some schools have tried allowing the udent to bring into the examination room any books e wishes this does not result in a significant improvement of the standard, and occasionally upsets the udents. At least two American departments pro eding on the theory that a student ought to know st what he knows, have tried allowing each student set himself a question and then answer it the sults were catastrophic and the experiments were not peated.

There is in fact a definite technique of answering say type questions a technique which comes naturally some people but has to be painfully acquired by others, ho may fail simply through lack of experience in it obody would pretend that justice is always done, and y modification of format or procedure which may sult in fewer injustices is worth consideration. Examina ons are not the only means by which the worth of a udent may be assessed and it is highly desirable that e should have a clear idea of what we are doing when we t and mark a written paper It is one of the benefits the introduction of the objective examination into edical affairs that it will force us to think again about e form in which our own papers are set

At present we must regard the medical objective amination as something which has still to prove its orth despite the interesting studies which are being dertaken on its relation to student proficiency But ere is little doubt in my mind that a generation of octors brought up on objective examinations will be fferent from the generation brought up on essay type estions, for the form of the examination not only tests e student, but also colours the way he works (Vernon 40). Whether they will be better or worse doctors is a estion nobody is likely to be able to answer for at least any years to come and one is tempted to say that ychology is gaining a measure of control over medical ucation through the weapon of achievement tests much in advance of its ability to evaluate the changes which it is introducing Nevertheless these changes are of the greatest interest, and deserve the closest consideration from every medical examiner As Vernon (1940) points out, neither type of examination can be considered satisfactory by an impartial observer but their faults to a certain extent cancel out It is perhaps to a combination of objective and essay questions in the same paper that we must look for future advances in the science of examining

I made these observations during a trip to the United States under the auspices of the Rockefeller Foundation, whose help I gratefully acknowledge I should also like to thank the National Board of Medical Examiners for permission to quote from their examination questions, the department of anatomy at the University of Rochester for the use of some of their questions, and Dr John T Cowles of the Educational Testing Service for his invaluable and patient assistance

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RESUSCITATION OF THE NEWBORN WITH INTRAGASTRIC OXYGEN

(AKERREN'S METHOD)

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IN contrast with the general decrease in infant mortality during the past fifty years the stillbirth rate and the neonatal death rate have remained obstinately resistant to improvement. Thus Smith (1951a) has reported that of every 10 000 births in the U.S.A some 150 lives are lost in stillbirth and a further 150 infants fail to climb out of what he has called the Valley of the Shadow of Birth.' In this country deaths in the first day of life still account for 38% of those occurring in the first month of life (the neonatal period)

One important cause of these deaths is asphyxia *neonatorum* Moreover of those who survive this dangerous complication not all escape damage to the central nervous system.

The establishment of respiration in the asphyxiated newborn infant is as much a problem today as ever Whatever primarily causes depression of the respiratory centres and prevents them from acting the delay or insufficiency of respiration itself deepens the anoxia with still further depression of the respiratory centres. The primary purpose of treatment is to prevent this additional secondary anoxia. Of the many different methods advocated and practised to combat asphyxia neonatorum no single one has received universal approval. Methods once popular have fallen into disfavour and others have been abandoned because they were found harmful The present tendency is toward gentle rather than vigorous stimulation, but, on the other hand, the apparatus and procedure devised for producing this stimulation have tended to become increasingly complex What is much needed is a method which is simple, safe, and effective, and ideally could be used in home confinements

One with claims to fulfil these criteria was reported by Akerren and Fürstenberg (1950), who described the resuscitation of asphyxiated newborn infants by passing oxygen into the stomach Ylppö (1935) had already shown that in premature infants oxygen in the alimentary tract is absorbed directly into the blood stream from the capillaries of the intestinal mucosa

We have been unable to find any account of the use of this method since the publication of Akerren's original article In this paper its use in 48 infants is reported

Method

It is the nurses in the labour ward who are confronted with the asphyxiated baby, and we have found it perfectly safe to entrust them with the decision to use Akerren's method Time is thus saved, and time is the important factor Normally, when the head is born, the inside of the mouth is wiped carefully with a square of soft linen, and mucus is aspirated from the pharynx with a mucus extractor As soon as the infant is born, the cord is tied and cut, and the infant is placed in a warm cot with a small pillow humped into the loins and with the head slightly lower than the feet, aspiration of mucus is then repeated if necessary By this time most infants will be breathing well If respiration is delayed, the tongue is firmly gripped with small pointed tongue forceps at least $^{1}/_{2}$ in from its tip, and gentle traction is applied If despite this the infant does not breathe or gives no more than an occasional gasp, and especially when the heart beat by becoming slower and feebler indicates that the infant's condition is deteriorating, then Akerren's method of resuscitation is applied If the infant is born white and shocked and shows no sign of immediate improvement, the method is used without delay It has taken the place of stimulants such as nikethamide and lobeline

In each labour ward is kept an autoclaved box containing four Jacques catheters, a pair each of sizes 5 and 3, one catheter of each pair serves as the inlet and has a glass connection for attachment to the pressure tubing of an oxygen cylinder The second of each pair serves as a safety or outlet catheter The pair appropriate for the size of the infant is chosen, and the safety catheter is passed first The stomach contents are aspirated, the nurses being satisfied that the response is better when this is done The upper end of this catheter is then placed under water in a small gallipot The inlet tube with the oxygen running through it is passed, and within a few moments the stream of bubbles in the gallipot shows that oxygen is entering and safely leaving the stomach The catheters are left in situ until spontaneous breathing is well established The abdomen is watched, and, as the oxygen enters, the stomach and sometimes the intestines may be seen to bulge With the oxygen running at 1 litre a minute, the abdomen was not unduly distended in any of the children in our series

First Trial

The first occasion when we used this method seems to us to merit a special description In 1949 Dr Akerren visited our hospital, and, just before leaving, mentioned his method modestly, indeed almost casually, to one of us (H K W) No trial was made of it for many months The notion of inflating the stomach of a severely shocked baby was startling Responsibility for making the first experiment could hardly be delegated to a resident, certainly not to a nurse, and the likelihood of being in the hospital at just the right moment for trying it was remote The project seemed impracticable as well involving risk It was allowed to pass out of mind

"The mind," wrote Wilfred Trotter (1941), "likes a idea as little as the body likes a strange protein, and it with a similar energy It would perhaps not be too f to say that a new idea is the most quickly acting known to Science"

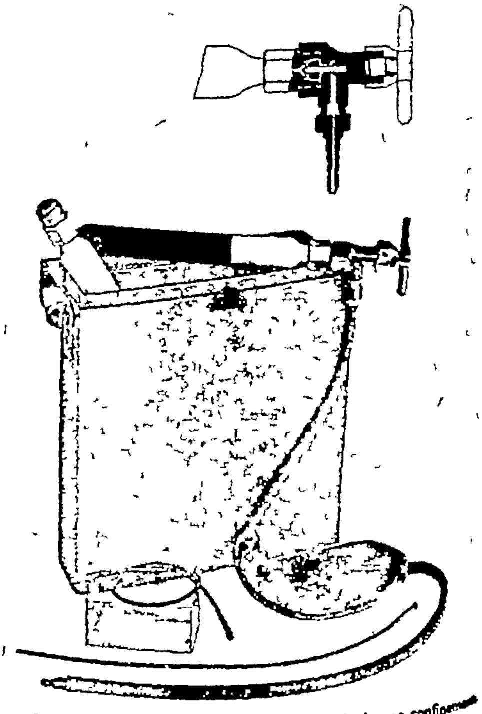
Even when the opportunity arose, this instinctive r tion, so comfortably rationalised, still delayed trial o method until its chance of success had become unfavourable as possible It is chastening to reflect had it failed on that occasion, we should have been than ever tempted to reject it finally So much by of apology to its originator The occasion of its trial as follows

A primigravida, aged 31, was delivered by Mr C K V after a labour lasting thirty hours Under open ether breech extraction was done by Lovesett's method, and were applied to the aftercoming head The infant was white and toneless The air passages were cleared, the was tied, and oxygen was directed through a tube into mouth at 4 litres a minute after the tongue had been forward The heart was beating at 70 a minute The gasp occurred after 5 minutes, and then at intervals of 40, and 30 seconds, giving hope that breathing was However, for half an hour there were only gasps weakened, became less frequent, and finally became imperceptible After 65 minutes the heart was irregularly at 35–40 a minute, and its sounds were only audible

It was at this point that Akerren's method came to Catheters and connections were quickly assembled, oxygen was passed into the stomach, whose distended was immediately seen through the lax abdominal wall minutes later (75 minutes after birth) the infant became pink, and full regular respirations were established with dramatic rapidity Thereafter the baby gave no cause further anxiety and when last seen at 3 years of age appeared to be developing normally

Experience of 47 Other Cases

After this favourable experience we decided to use method whenever severe asphyxia did not respond the routine procedures described In the



Apparatus for the resuscitation of the newborn in home confinem ries of 48 infants so treated 7 did not respond 41 re resuscitated, but 3 subsequently died (at $1^{3}/_{4}$ hours hours, and $2^{1}/_{2}$ days) In those that responded the ual sequence of events was a change in the infant's lour to pink, followed by the onset of breathing at a riable time In our series this ranged from 1 to 75 nutes. The accompanying table shows that most of e infants were breathing within five minutes though 2 ok as long as an hour

nutes before breathing ygen	1	2	3	4	5	10	15	15+
mber of infants	14	6	7	0	3	3	3	6

At necropsy severe cerebral damage was found in 3 bies and in the remaining 7 the only findings were lectasis and evidence of asphyxia.

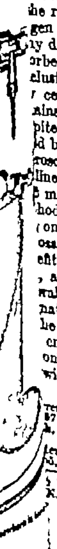
Apparatus for Home Confinements

As oxygen is usually available only in hospitals the actice of this method is at present restricted. Accord ly we have devised a miniature portable cylinder* e figure) which could be included in the general practi ner's or the midwife's equipment It is supplied in an dily portable box containing two miniature cylinders screw tap, rubber tubing a pressure bag and two ques catheters; the box and contents weigh 5 lb e tap is screwed on to the cylinder and the handle is ned in a clockwise direction; this drives a piercer the cap whereupon oxygen fills the bag and then s out at 1 litre a minute There is enough oxygen in h cylinder to give a continuous supply for 20 minutes. s equipment will we hope, enable the doctor or the wife to apply this method of resuscitation in the home

Discussion

n spite of the large amount of experimental work way in which respiration is initiated in the newborn ant is still not clearly understood. Moderate anoxia sensory stimuli are the main factors (Smith 1951b) for any reason respiration is not established, the tinued anoxia leads not to stimulus but inevitably greater depression of the respiratory centres, with less likelihood of the establishment of breathing aim of treatment, therefore is to prevent this ression by supplying oxygen, although this cannot course directly affect the primary cause of failure he respiratory centres to function The delivery of gen to the respiratory centres has been the aim of y different resuscitative measures That it is rapidly orbed from the gastro intestinal tract has been clusively demonstrated, but what makes the respira centres respond in one child and not in another ains a problem, as is illustrated by the cases when, pite of our endeavours, no cause for failure to respond d be found either clinically or at necropsy No roscopic examination was made for the presence of line membrane

may be objected that the claim made here for this hod could be established only by a controlled study once it was found to be clinically effective, it became ssible to withhold it from any infant who might be efited. In our experience Akerren's method is simple and effective We have also used it successfully ral times for the treatment of severe cyanotic attacks in nature infants as originally practised by Ylppö (1935) he miniature light weight oxygen container described enable this method of resuscitation to be practised only in hospitals, as at present, but also in domiciliary wifery



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THE MANAGEMENT OF POSTMATURITY

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> Make no more pretence
> "Of new discoveries whilst yet thine own
> 'And nearest little world is still unknown."
> GEORGE HERBERT *Travels at Home* 1633

THE title of this paper, though not strictly accurate, is reasonably apposite. Actually this is a study of cases in which pregnancy was prolonged past the expected date of confinement calculated by Naegele's rule.

In the present state of knowledge it is impossible to make an exact clinical study of postmaturity owing to the lack of any clear definition and to the difficulties in diagnosis Possibly because of these difficulties, and because postmaturity and prolongation of pregnancy are often accepted as synonymous there is a wide variation of views on the importance of this subject. Kamperman (1948) says that postmaturity is a state of mind of the obstetrician in most clinics the problem is not considered important enough to deserve much study and Holmes (1948) says that "Postmaturity is a figment of the imagination On the other hand many workers hold that postmaturity is important.

It might be supposed that the problem could easily be solved by simple pragmatic methods, such as the study of fœtal mortality figures. The obvious difficulties to this are the lack of exact definition of postmaturity and the obscurity of diagnosis It is for this reason that we have investigated postmaturity in relation to the expected date of confinement estimated from the last menstrual period by Naegele's rule. We fully realise that this method is not free from error as regards postmaturity This study however, is concerned not with postmaturity in its exact sense but as to whether it matters if a woman has her confinement at the expected date or later We believe that in women who are reasonably certain of the date of their last menstrual period, and after a correction has been made for a menstrual cycle longer than twenty-eight days, this rule is still the most useful guide in the management of these cases. It has the additional advantage of requiring no exceptional skill or any special methods and can therefore be used by practitioners everywhere.

We are aware that this scheme of management is open to the criticism that each case is not treated individually But individual treatment, avoiding routine induction is a counsel of perfection, and, though it may become possible in the future, is not applicable in the present state of knowledge In fact, slavish adherence to individual treatment is a cause of the high fœtal mortality in postmaturity

A few workers (Clayton 1941 McKiddie 1949 Hamilton 1950, Latto 1951 Rathbun 1943) have published reports on the fœtal mortality in pregnancies prolonged past the expected date of confinement, and almost without exception they show an increase in the fœtal mortality Latto (1951) and Rathbun (1943) by excluding certain cases seek to show that the increase is not in fact substantial but they offer no conclusive evidence to justify the exclusion of these cases. As corrected figures are always debatable we have made no correction in our study and we hope that if others can be interested to carry out similar investigations, it will be possible to gather series large enough to make correction unnecessary

Method

In our investigation at Park Hospital we divided the patients attending our antenatal clinic into two groups by nothing more eclectic than which clinic they attended—either that of one of us (D C R) or of one of his colleagues who kindly allowed his cases to be used for this study In one group, called the induced group, the patients were admitted on the day before the expected date of confinement, on which day they were given such simple stimulants as a hot bath and an enema, but no drugs, and, if labour had not started on the next day, the membranes were artificially ruptured There was absolutely no obstetrical selection in either group For example, in the induced group labour was induced whether the women were primigravidæ or multiparæ, whether the head was engaged or high and mobile, and even if there was a breech presentation In a few of the earlier cases the patients were given 'Pituitrin' on the expected date of confinement, but this practice was discontinued for the reason discussed below

TABLE I—FŒTAL MORTALITY DUE TO STILLBIRTHS

Group	No of cases	No of stillbirths
Controls (mature at term)	1229	19 (*1 54%*)
Induced group	203	3 (*1 47%*)
Postmature group	410	19 (*4 63%*)

In the second group, called the postmature group, the women were allowed to continue to spontaneous labour unless, as happened in a few cases, labour was induced for some other obstetric reason

A third group of cases acted as controls, these were the unselected cases of natural delivery at term in the past two years—term for this purpose being from seven days before to seven days after the expected date of confinement

As regards the induced cases we do not suggest that the results could not be equalled or even possibly improved by allowing an interval of seven to ten days to elapse after the expected date of confinement, as suggested by Mills (1950) To find this safe margin further study is required We chose the day after the expected date of confinement to induce labour because we felt that some starting-point was needed, and because, if our results were reasonable, it would provide a ready answer to those who might argue that we would have a high proportion of premature babies

Results

Table I shows the fœtal mortality due to stillbirths The postmature cases in this table were more than seven days past the expected date of confinement They outnumber the induced group simply because the resident staff, who see a large number of the cases, often did not arrange for their admission on the correct date, the routine being new to them

TABLE II—STILLBIRTH RATES IN POSTMATURE CASES

Postmaturity	No of cases	Stillbirths
From 7 to 13 days	261	6 (*2 31%*)
14 days or more	149	13 (*8 72%*)

Table II shows the difference in stillbirth rates between postmature cases up to fourteen days past the expected date of confinement and those more than fourteen days past it The differences between the fœtal mortality-rates of the postmature groups and between the induced group and the group in which the postmaturity was more than 14 days are statistically significant Table III shows the degree of agreement between our figures for stillbirth-ra [illegible]d those published by other workers Table IV gives the incidence of postmaturity both in our own c and in those published by other workers

TABLE III—COMPARISON OF STILLBIRTH RATES

Authority	No of post mature cases	Stillbirth rate		Criteria of post maturity
		Mature cases	Post-mature cases	
Hamilton (1950)	171		8 2	291 days
Latto (1951)	171		5 2	294 days
McKiddie (1949)		1 3	2 8	287 days
Clayton (1941)		4 25	6 15	291 days
Present investigation	410	1·54	4·63	287 days
" "	149	1 54	8 72	294 days

There was 1 cæsarean section in the induced and 8 in the postmature group The instrum rate in the induced group was less than half that in postmature group This is in agreement with Clay (1941), McKiddie (1949), Hamilton (1950), Latto (195 and Rathbun (1943) In the postmature group were 3 deaths in utero before the onset of labour

In the induced group containing 203 cases it necessary to rupture the membranes in 162 cases. T interval from the time the membranes were rupt until delivery was as follows less than twenty-f hours 61 cases, from twenty four to forty-eight h 70 cases, and more than forty-eight hours 31 c The interval between the rupture of the memb and the onset of labour, judged by the start of re pains, was more than forty eight hours in 10 ca two to five days in 5 cases, six days in 3 cases, seven days in 2 cases One of us (D C R) was through illness for a long time when these cases occ and owing to a misunderstanding no uterine-stim drugs were used, if they had been used, several of long intervals might have been avoided One o 3 fœtal deaths took place in a case in which the memb were ruptured for a hundred and fifty hours b delivery In 16 cases labour lasted more than hours The smallest baby in the induced group w 5 4 lb The average birth weight was almost e equal to that of the controls

TABLE IV—INCIDENCE OF POSTMATURITY

Authority	Incidence %	
	Criterion 287 days	Criter 291 da
Gibson and McKeown (1950)	31 72	
McKiddie (1949)	24 10	7 3
Clayton (1941)		3 (
Latto (1951)	25 20	9 (
Present investigation		

As will be seen from the combined figures tables, the fœtal mortality for cases fourteen d more overdue is about 7% If the incidence of cases is also about 7%, on an annual birth rate of 8 the fœtal mortality is about 3920 per annum fœtal mortality for the induced cases can be by further work to correspond to our figure of le 2%, the yearly fœtal salvage would be about 3 annum, a rather startling figure

Discussion

Our reasons for making this investigation were felt that the question of postmaturity needed cl and we wished to assemble evidence on which to management of these cases Our argument follows

(1) It is impossible at present to diagnose post either clinically or radiologically with anything a ing sufficient accuracy upon which to base any tr

(2) It follows that it is impossible to treat all the cases dividually What is really necessary before cases can e treated individually is an accurate method of detecting rly and minor degrees of deterioration of the fœtal ondition in utero

(3) There is strong theoretical evidence that the etal environment deteriorates after term That some etal deaths after term are due to malpresentations or to ng and difficult labour rather than to intra uterine ysiological changes alone, or to a combination of these o factors does not in any way affect the main issue.

(4) Therefore labour should be induced at or after a rtain interval following the expected date of confinement. We believe that a certain degree of prematurity preferable to the same degree of postmaturity The terval that can safely be allowed after the expected ate of confinement is a matter for further investigations. rom our present knowledge we feel that it will probably ove to be about seven to ten days

Not one of the criteria commonly used in the diagnosis maturity can definitely foretell when it has been ached Even if they are all used, the margin of error a few days therefore they cannot be used as a certain ride to treatment These criteria are

(1) The calculation of the expected date of confinement the Naegele rule This has already been discussed
(2) Estimation from a single coitus
(3) The growth of the uterus.
(4) The date of quickening
(5) The size of the foetus
(6) The feel of the fœtal skull on combined abdominal d vaginal examination
(7) Rigidity of the foetus
(8) Oligohydramnios.
(9) The condition of the cervix
(10) Radiology
(11) A test induction with pituitrin.

Rigidity of the fœtus due to increased tone in the eletal muscles, and oligohydramnios have been phasised by Wrigley (1046) as important signs t can anyone really assess the tone of the fœtal scles or a decrease of liquor accurately enough to stify embarking on a certain course of treatment of such portance ? We have specially looked for these signs, d although we agree with Wrigley that oligohydramnios y at times be marked, its occurrence is irregular and th signs are usually too esoteric to have any value as a ide to treatment.

As regards *radiology* there are still no signs either centres of ossification or in skeletal configuration ich can be used as accurate criteria of postmaturity

Some workers state that *pituitrin* and *pilocin* are y effective when the foetus is mature, and can therefore used to test maturity We have no real information this subject ; but, apart from a few early cases in present series we have not used pituitrin as part of a ical induction We have, of course, used it in the t, but we felt that it would not help us in the present estigation, owing to doubt about its action. In es in which it is given and has no effect one cannot certain that the reason for this is that they are not term, until it can be shown that pituitrin always mulates the uterus at term in every case

We therefore feel that, apart from the cases where ere is an obvious discrepancy between the signs and mptoms and the expected date of confinement, these ns and symptoms of postmaturity have not the ue that some impute to them We agree that when eral of these signs are present together one can ten presume postmaturity with reasonable confidence t they still tell us very little about the health of the tus and in the many cases in which they are absent are virtually helpless unless we have a scheme of nagement such as the one we propose We only gest such a scheme until more accurate diagnosis out the fœtal condition renders it unnecessary

We shall not discuss in detail all the physiological factors which may endanger the life of the fœtus in utero It is now fairly generally agreed that the fœtal environment deteriorates after term to illustrate this deterioration we cite (under the heading of Bibliography) a few of the many recent publications on fœtal asphyxia Of the many factors involved—e g the fœtal and maternal circulation the efficiency of the placenta and placental reserve and the transference of metabolites and electrolytes—the factor which is most easily understood and which appears to be most important is fœtal asphyxia A great deal of work has been done on this subject tending to show that the oxygen content and saturation of the fœtal blood decrease after term

Walker (1053) found that at the 30th week of pregnancy the average oxygen content in the umbilical vein was at least 14 vols. % with a saturation of 70% The arterial content and saturation were roughly half the venous. At the 39th week the oxygen content was reduced to 12·4 vols. %, giving a saturation of 60%. At 42 and 43 weeks the venous oxygen content was, on the average as low as 6–9 vols %, the saturation being 30–40% An important finding of Walker's was that throughout pregnancy the difference in oxygen content between fœtal arterial and venous blood remained very constant at about 5–7 vols. %.

From Walker's work it is evident that if the venous content diminishes to 6–0 vols % as it often does after term, the arterial oxygen content will be so low that the life of the fœtus is in jeopardy Thus must lead to especial danger if the labour is in any way difficult or prolonged. We are not in a position to comment on the importance of this theoretical hazard but there is little doubt from a practical standpoint that the fœtal mortality is increased after the expected date of confinement (Clayton 1941, McKiddie 1949, Hamilton 1950 Latto 1951 Rathbun 1043)

If these hypotheses are accepted it follows that it is safer in the present state of our knowledge to treat cases according to some rule rather than individually We realise that this is unsatisfactory but feel that it is much safer until such time as we can judge the condition of the fœtus in utero In cases which appear quite normal the fœtal condition may be deteriorating dangerously Wrigley (1946) scathingly quotes the reply of students at two London medical schools when asked how they would treat patients who were overdue When 14 days have elapsed labour should be induced According to Wrigley This reply is as fatuous as it is dangerous.' But is it ? Though we do not know the exact interval that can be safely allowed after the expected date of confinement, it appears from the few figures available to be about fourteen days though possibly this is rather too long Surely it is a very much safer plan to induce labour then than to rely on such exiguous signs as rigidity and oligohydramnios

In brief our suggested plan for managing these cases is that, except in cases where there is serious doubt about the history it is dangerous to allow a woman to exceed her expected date of confinement by more than a short period and that after that period labour should be induced What that period is we hope that further work will show but it seems to be about seven days. In trying so learn more about this problem we shall be well advised to keep in mind Cardinal Newman's dictum that the logic of facts is the most thorough teacher '

Summary

Two series of cases in which pregnancy was continued past the expected date of confinement were studied In one group labour was induced a day later by rupture of the membranes and in the other group the pregnancy was allowed to continue until the onset of spontaneous labour

The results as regards fœtal mortality were very much better in the induced group and the inductions did not appear to give rise to any additional hazard or difficulty

It is therefore suggested that, in the present state of our knowledge, these cases should be treated by routine induction rather than individually

We hope that further work will show what period, if any, can be safely allowed after the expected date of confinement At present we think it will probably be about seven days

We wish to thank Dr W R Addis for his kindness in allowing certain patients under his care to be used in this investigation, and Dr S R A Ayling, Dr B Didsbury, Dr D D Davies, Miss J K. M. Clift, and Miss B E Batty for their invaluable assistance in inducing labour in many of the cases

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"REACTIONS" TO DEXTRAN

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IN 1949 Thorsen reported that in Sweden the incidence of reactions of all types associated with the infusion of solutions of dextran was only 0 8%, compared with 8 2% of reactions after blood-transfusions A similar freedom from undesirable effects has been the experience of one of us (A W W) after giving more than 500 infusions of dextran solution of both Swedish (Pharmacia) and British (Benger) manufacture in the treatment of various hypotensive states in surgical patients This low incidence of reactions associated with the use of dextran has been regarded as one of its most important advantages as a substitute for plasma However, Pulaski (1951) reported a reaction-rate of 40% when Swedish dextran was injected into normal soldiers, and in 1952 Thorsen (personal communication) also found that reactions commonly followed the infusion of Swedish dextran solutions into normal volunteers No satisfactory explanation has been given of the rarity of all types of reactions when dextran is infused into patients whose blood volume has been reduced by the loss of blood or plasma, and of their relative frequency when the recipient's blood volume is normal

In 1952 a highly fractionated preparation of dextran became available in which 65% of the material was of molecular weight between 130,000 and 250,000, and more than 40 litres of this preparation has been infused by one of us (A W W) into shocked patients, with only two mild and transient reactions It was decided to repeat the experiments of Thorsen and of Pulaski by infusing some of this solution into normal volunteers to see if it produced a high rate of reactions when the blood volume was within normal limits

Methods

The five volunteers were healthy, fully grown males aged 21–38 They were recumbent for half an hour before and throughout the infusion and for a time thereafter Blood was withdrawn from a vein the left forearm, and the infusion of dextran was through the same needle, the duration of the varied from 500 ml in 47 minutes to 1 litre in 11 four of the volunteers received 1 litre, and the 500 ml of solution Further samples of venous were withdrawn about 10 minutes after the infusion finished and at short intervals during the first 6 at 24 hours, and daily thereafter The volume was measured in four volunteers on treated with Wintrobe oxalate mixture and then fuged at 3000 r p m for 20 minutes The each blood sample was allowed to clot The total protein level was determined by the micro Kje method of Ma and Zuazaga (1942) after pr with trichloro acetic acid. Albumin was determined in the filtrate after saturation of the with magnesium sulphate (Popjak and McCarthy 19 Dextran was measured by a modification of the anth method of Bloom and Willcox (1951) The bl was emptied before the infusion began, and urine collected in 6 hour specimens during the first four d and in 24 hour specimens thereafter, and the vol and dextran concentration (modified anthrone metho Bloom and Willcox (1951)) were measured The pulse and systolic and diastolic blood-pressures were repeat measured before, during, and after the infusions dextran, and the skin and general state of the volunt were closely observed

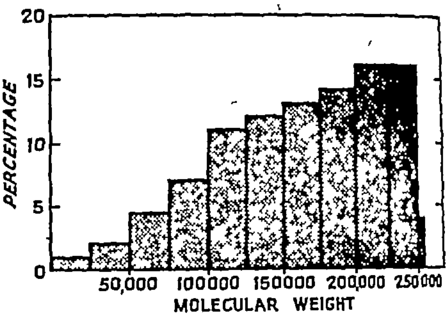


Fig 1—Distribution of molecular weights of 6% dextran solution

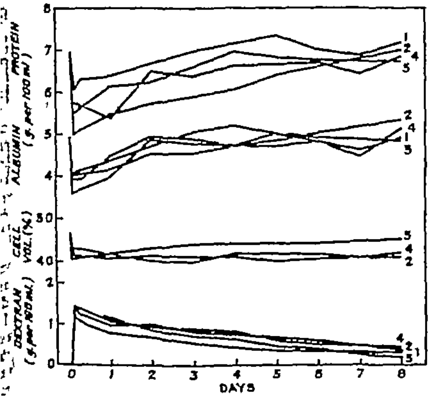
The solution (batch 3715/3/ex 225) contained dextran in 0 9% saline solution and had the mole composition indicated in fig 1 The crude dextran prepared by the action of *Leuconostoc mesenter* on sucrose

Results

"*Reactions*"

Reactions of various degrees of severity developed all five volunteers Wealing, redness, and the skin appeared in places where there was on the skin—e g, under the neckband of the shirt, tops of the socks, the trouser waistband, and sphygmomanometer cuff In two volunteers these appeared after the infusion of about 700 ml., and in others 20 and 60 minutes after completion of the infu The wealing persisted for periods of up to $2\frac{1}{2}$ h A sensation of fullness of the head was felt by volunteers, in two there was also flushing of the and in one of these puffiness of the eyelids, espe towards the end of the infusion Two noticed retrost pain during the infusion, and two experienced nau In three there was a sensation of illness and fullness the chest, which began when the skin reactions subsiding and lasted for about two hours

After completion of the infusions change in was followed by vasomotor disturbances which in volunteer were thought to be vasovagal, but only this one instance was improvement produced by the head In a second volunteer lowering the head he disturbance more severe All four volunteers who xperienced this reaction could stand up without ill ffects from about five hours after the end of the infusion ut at this time three were euphoric and all felt 'ill' n various ways They experienced 'pounding" and ullness in the head and chest which were made worse y even minor exertion, tolerance to exercise was much educed, and breathlessness developed on climbing a hort flight of stairs and persisted to various degrees or a week or more after the infusion



ig. 2—Changes in serum-total protein serum-albumin and serum-dextran levels and in packed-cell volume in the four volunteers who eceived 1000 ml of 6% dextran solution.

lood-pressure and Pulse rate

So long as the volunteers remained recumbent there ere only slight alterations in systolic and diastolic ood pressure and in pulse rate When volunteer 1 sat an hour after the end of the infusion and hung his gs over the side of the table there was a very rapid ll in systolic blood pressure from 148 to 70 mm Hg e diastolic pressure fell from 100 mm Hg to an recordable level, and the pulse rate rose from 80 to er 120 a minute; when he lay down the blood pressure d the pulse-rate returned to their previous values milar but less pronounced reactions developed in the her volunteers, except that in volunteer 2 the pulse rate ll when the blood pressure fell.

inary Excretion of Dextran

Two volunteers excreted 6% of the injected dose of xtran within two hours of the end of the infusion d within eighteen hours three had excreted 10% and e other two 8% of the dose The total quantity creted in the urine during the 48 hours after the infu n ranged from 8 to 11% after 48 hours there was o little dextran in the urine to be measured accurately

hanges in the Blood

Fig 2 shows some of the changes in packed-cell volume d the serum levels of total protein albumin and xtran during the eight days following the infusion of litre of 6% dextran solution into four volunteers e initial reduction of total protein in the serum was out equal to the initial increase in serum-dextran level ereafter the serum dextran level declined steadily; t, although within 4 days in three volunteers the levels both total protein and albumin rose above their tial values, the packed-cell volume was below the tial value after eight days

The changes during the first 24 hours after the infusion 1 litre of dextran into volunteer 4 are shown in more detail in fig 3 During the first 8 hours there were distinct changes in packed-cell volume but only slight fluctuation in the serum levels of total protein albumin and dextran Similar rapid changes in packed cell volume in the absence of reactions have been observed previously by one of us (A W W) in shocked patients after infusions of dextran and by Thorsen (1949) after the infusion of Swedish dextran.

Such pronounced alterations in cell concentration occurring during the estimation of plasma volume by the dye-dilution method caused wide discrepancies in the volumes obtained and it was thought wiser to discard the results of these direct measurements of plasma volume

The plasma volume of a normal adult male is 7% of the total body water which in turn is 60% of the 'ideal' body weight for a particular age sex and height plasma volume is thus 4·2% of 'ideal' body weight Plasma volume was calculated from their 'ideal' body weight for volunteers 2 4 and 5 who each received a litre of dextran solution From this calculated plasma volume and the observed packed cell volume before the dextran was infused the total volume of red cells in circulation was calculated Since Meyer et al (1952) using P^{32} did not find any significant alteration in red-cell volume after the infusion of a litre of dextran into normal people it was assumed that in our volunteers the total red-cell volume remained constant during and after the dextran infusion, and the subsequent changes in plasma volume were calculated from the observed changes in packed-cell volume. From these plasma volumes a good approximation of the variations in the total quantities of total protein, albumin and dextran in circulation within the vessels can be obtained The results obtained in volunteer 4 are shown in fig 4

In three of our volunteers the increase in plasma volume immediately after the completion of the infusion of a litre of dextran solution was 800 ml, 1000 ml and 1300 ml similar large increments have been reported by Haynes and DeBakey (1951) and Meyer et al (1952) Within about 2½ hours however, the plasma volume in each of our volunteers had diminished to less than that before the infusion of dextran was begun By 24 hours after the infusion the plasma volume once more had risen well above the initial volume and this increase

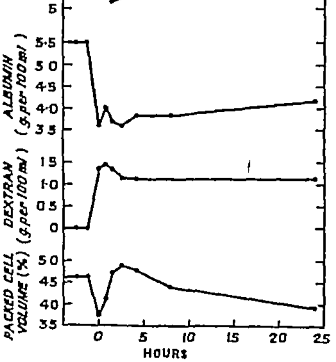


Fig 3—Volunteer 4: detailed changes in serum-total protein, serum-albumin and serum-dextran levels and in packed-cell volume during the first 24 hours after infusion of 1000 ml. of 6% dextran solution.

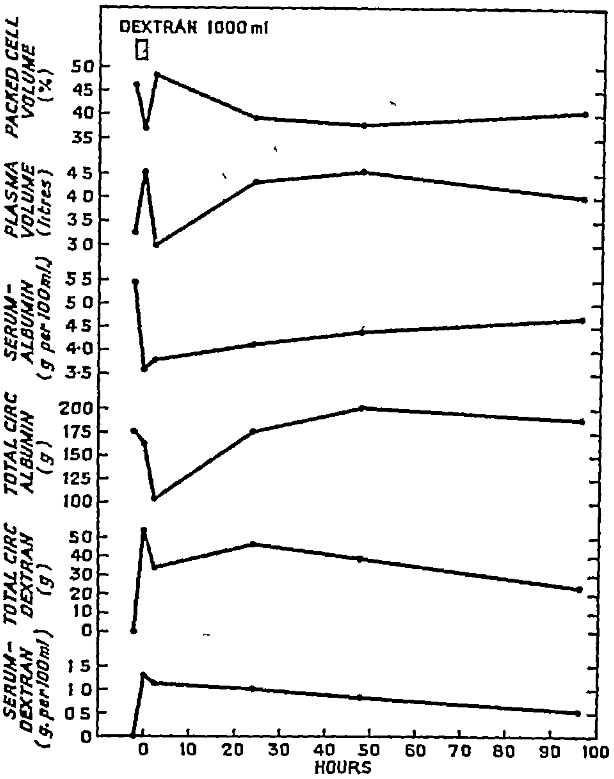


Fig 4—Volunteer 4 changes in packed-cell and plasma volumes, serum-albumin and serum-dextran levels, and quantities of total circulating albumin and dextran after infusion of 1000 ml of 6% dextran solution

was maintained at 48 and 96 hours Immediately after the completion of the dextran infusion there seemed to be very little alteration in the quantity of serum total protein and serum albumin in circulation, although the concentrations of these fractions were greatly reduced However, $2^1/_2$ hours later up to more than 30% of the initial quantity in circulation of total protein and up to more than 40 per cent of the initial quantity of circulating albumin had left the vessels During this period there was also a loss of up to 30% of the dextran present at the end of the infusion

During the period from $2^1/_2$ to 24 hours the plasma volume again increased and the total quantities of total protein, albumin, and dextran circulating in the serum also increased, but their concentrations remained low From 48 hours onwards there appeared to be more total serum protein and albumin in circulation than before dextran was administered

Discussion

There appeared to be two distinct phases in the "reactions" which the present volunteers exhibited The first was characterised by urticaria, it began during or soon after the infusion was completed and lasted for various periods up to two hours or more after the infusion ceased The second phase was characterised by vasomotor instability, it usually began after the infusion had been completed, and appeared to be related in time to the rapid increase in packed-cell volume and the underlying pronounced reduction in plasma volume, as the packed cell volume decreased and the plasma volume increased, the tendency to acute vasomotor disturbance declined

Thorsen (1949) and Bull et al (1949) explained the reduction in albumin and total-protein levels during the week after dextran infusion as being due to osmotic [illegible]sion of albumin by the circulating dextran It [illegible] it appears likely that at this time there may be more rather than less albumin in circulation. The prolonged increase in plasma volume indicated by calculations is in accord with the greatly reduced exer tolerance, precordial pain, fullness of the head, breathlessness on exertion exhibited by these volunte with the slow fall in the plasma dextran level and the small urinary excretion of dextran

Summary

A 6% solution of dextran in 0 9% saline solution infused into five normal volunteers, of whom received 1000 ml and one received 500 ml

The rapid initial increase in plasma volume, of plasma proteins, and decrease in packed-cell induced by these infusions were followed by the movement out of the vessels of up to 30% of the circulating plasma protein and infused dextran- W 12 hours this transfer was reversed, and the pl volume and the total quantities of plasma protein dextran in circulation were increased

"Reactions" were produced in each of the volunteers These reactions have been resolved two phases the first, characterised by urti developed during or soon after the infusion was comp and lasted for up to 2 hours, the second, by vasomotor instability, developed after the was completed and appears to be related to rap reduction in the volume of plasma in circulation.

We are indebted to the volunteers who submitted to investigations, and to Benger's Laboratories Ltd. for a sup of dextran solution and for data regarding its composit

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THE RISKS OF TONSILLECTOMY

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Tonsillectomy occupies a curious place in It is one of the commonest of all items on the ope list of any hospital, for many thousands of tonsillect are done every year in England, but every surgeon a tonsillectomy with anxiety, for the risk is always in his mind Before the late war the mortality cited one London centre was 1 in 1000, but figures do accurately reflect the difficulties, nor do they the conditions in small hospitals, where both sur and anæsthetist may be less skilled than in a centre

The account of the cases which follow form the ence of one surgeon, they were not all his own for some were under the care of colleagues, but disaster was so unusual and so tragic that it was rec in detail and discussed by the whole hospital staff therefore could fairly be said to have entered the ence of everyone on the spot, whether directly with the case or not

Before discussing the case records in detail, it might useful to contrast the risks of tonsillectomy at present time with those of twenty years ago There one risk, for instance, which has nearly disappeared chance of serious infection Before the discovery penicillin, an otitis media was quite common tonsillectomy in children, and many of the older surgeons can remember a subsequent death from meningitis Serious infection after tonsillectomy is now rare, although penicillin is seldom given beforehand as a precaution. Perhaps penicillin has made the wards safer for a serious cross infection of any kind is now unusual The anæsthetic risk also is less now when the anæsthetist is of specialist rank but more will be said about this later , a surgeon naturally cannot make expert comment on the anæsthetics of the present day but he has, at all events, as great an interest in their success as any other worker in the theatre

The risks can be divided into four groups—those at the time of operation those immediately after operation, those within twenty four hours, and those later than twenty four hours after operation

Anæsthesia

The surgeon needs for tonsillectomy a patient who is deeply anæsthetised and has had a smooth induction of anæsthesia A light anæsthesia and a troublesome induction both increase the bleeding and a glance at the patient when he is wheeled into the theatre from the anæsthetic room is enough to enable the surgeon to make a fair guess at the difficulty of operation provided that there is no peritonsillar fibrosis

Sudden death from the use of too much anæsthetic has not happened in my experience although it is a risk which might occur to anyone who considers the operation The difficulty has lain in the opposite direction, for I find the inexpert keep their patients under too light anæsthesia. Davis s or Boyle's gag is a traditional instrument and a trap for the beginner for no-one can anæsthetise an adult through the tube built into the gag if he uses ether alone and a child needs a very large flow of ether and even then steadily regains consciousness throughout the operation if he is well grown The best anæsthetic I have seen for tonsillectomy is intravenous thiopentone combined with an intratracheal tube which delivers oxygen

Risks at Operation

The risk *which is uppermost in the mind of the surgeon* is hæmorrhage Hæmorrhage at operation is likely if there has been a recent infection—e.g a sore throat, and a cold—or if there has been a peritonsillar cellulitis at any time, because of the resulting peritonsillar fibrosis.

The details of ligature of vessels in the tonsillar bed would be out of place in this article but the methods of dealing with severe hæmorrhage must be listed—they are in order a ligature introduced into the tonsillar bed with a curved needle suture of the anterior and posterior pillars, and suture of the pillars over a gauze swab If hæmorrhage is severe the operation may, rarely have to be abandoned.

A young doctor had been in bed a month before with a severe quinsy and had only recovered from the infection a fortnight before admission to hospital for tonsillectomy He bled so freely that onlookers thought he might die on the table in spite of two blood transfusions. The surgeon succeeded in removing only one tonsil but managed to stop the bleeding by ligatures over a gauze swab The other tonsil was removed two months later without incident

The mistake here was to try to remove the tonsils too soon after a quinsy Tonsillectomy is always difficult when there has been a quinsy because of the fibrosis which prevents the cut blood vessels from retracting but if an adequate time—e.g six weeks—is allowed to pass before operation is undertaken, the surgeon s task will be easier

It is unfortunately true that the neater the surgical work the greater is the risk of bleeding at the time of operation or in the first twenty four hours Serious bleeding *for example is less common after* a guillotine operation than after complete dissection This is not to be taken as a recommendation of the guillotine operation The risk of hæmorrhage after tonsillectomy with scissors is only slightly greater than after blunt dissection and there is no doubt that the patient feels more comfortable if his tonsils have been cut out with a sharp instrument I vary my practice in this detail and use scissors in London and a blunt dissector in the country, but never the guillotine The following incident illustrates the risk of sharp dissection

A surgeon of international reputation was asked to visit a foreign country shortly after the war to demonstrate his method of tonsillectomy which relies chiefly *on the use of scissors. He operated on four cases, and the onlookers said* afterwards that they had never seen the tonsils so cleanly and neatly removed Unfortunately three out of the four patients bled within twenty four hours of operation. The surgeon had of course kept all four patients on the operating table until he was satisfied that the immediate bleeding had stopped for this is the present custom no matter which technique is used.

An example of a mistake of routine is the following

A child was admitted for tonsillectomy which was undertaken on the day following admission. The house-surgeon removed the tonsils without incident but, when he used the adenoid curette there was profuse bleeding He pushed the sucker tip into the nasopharynx, but it quickly became blocked so he abandoned it and used the sucker tubing alone to remove the blood At this point the child suddenly collapsed and died Nothing was found at necropsy to explain the sudden death but inquiry showed that the child had had a temperature of 99 6 F on the night of admission. This should have been enough to make the house-surgeon postpone operation He would have been wise also to have tried pressure with gauze before he used the sucker

The general rule is that no-one should be prepared for operation if his temperature has been higher than 99°F on the preceding evening Many people have a slight *temperature on admission (possibly from anxiety in strange surroundings)*; hence a temperature of 99°F can be ignored, but a higher temperature must stop a deliberate operation like tonsillectomy

The next period of risk is during recovery from the anæsthetic The position of a patient in bed after operation is generally agreed he should be on his side with his face visible and both hands should be in front of the chest. A good way to keep this position is to flex the leg which lies underneath. If the patient is not on his side and the airway is not free, there is a risk of sudden death from asphyxia by the tongue falling back

A surgeon of considerable experience joined the Services at the beginning of the war He removed the tonsils of a patient in the usual way and returned to the sister s room for a cup of tea. Ten minutes later he went to the ward where his patient was lying and found the bed surrounded with screens He asked why this had been done and was told that it was the custom to surround the bed with screens in the general ward when a patient was recovering from an anæsthetic. The surgeon was not satisfied and went to examine the patient behind the screens. He found that he had rolled on his back and was dead.

The lesson of this case, which is recognised in most hospitals is that a patient must be watched continuously until he recovers from an anæsthetic So far from screens being used he should be left in a bed where everyone entering a ward can see him unless there are enough available nurses for one to remain at his bed When a patient begins to recover consciousness he becomes restless and coughs out the airway A trained person must be by the bedside from this point until consciousness is complete to watch the breathing and to report unusual bleeding (there is always a small amount of blood coughed out during recovery and experience is needed to tell whether it is due to active bleeding or not) Maintenance of the airway may need a tongue clip and a gag such as Mason s gag which should lie by the patient's bed together with a sucker and rubber tubing

If active *bleeding is noticed just* before complete consciousness returns the patient should be brought back to the theatre at once

A man of 45 was admitted for tonsillectomy His tonsils were removed with little trouble, and he was sent back to the ward Word, was, however, sent twenty minutes later that the bleeding was more than usual The surgeon went to the ward and confirmed the message, so the patient was returned to the theatre, where a bleeding vessel in the right tonsillar fossa was found and ligatured There was no more trouble, and the patient knew nothing of his mishap

The important fact of this story is the stage at which the bleeding was discovered If a second operation has to be undertaken for hæmorrhage, the best time is certainly before recovery from the first operation

The next story is exceptional

A girl of 11 was admitted for removal of adenoid remains The anæsthesia was not entirely satisfactory, for the child was not deeply unconscious The adenoids were, however, removed, and the patient was sent back to the ward An urgent message was sent from the ward during the next case to say that the child had stopped breathing, and that the pulse could not be felt She did not recover, in spite of emergency bronchoscopy At necropsy a piece of adenoid tissue was found in the right bronchus

The adenoid tissue had certainly caused death from shock by sudden inhalation This rare accident might have been avoided if a guarded curette had been used for a guarded curette catches with its teeth any adenoid tissue which is cut by the blade The only objection to the use of a guard is that it tears the posterior pharyngeal wall, sometimes severely

It is remarkable that the lungs are seldom injured in tonsillectomy, although the surgeon works at the entrance to the whole bronchial tree In spite of great care a small amount of blood must be inhaled at every tonsillectomy, for X rays have shown traces of 'Lipiodol' at the lung base, when gauze swabs soaked in lipiodol have been used experimentally instead of the usual tonsil swabs

The lung seems to be able to dispose of a small quantity of blood, and I know of no record in England of a lung abscess due to blood-clot Rarely, inhalation of blood can cause pyrexia for ten days or a fortnight

Hæmorrhage after Return of Consciousness and within Twenty-four Hours

Hæmorrhage within twenty-four hours after an operation is the terror of all who look after cases of tonsillectomy—surgeon, anæsthetist, and nurses alike Within an hour a healthy patient may become desperately ill, unless he has urgent and expert treatment Every surgeon has had a case where a disaster has occurred after-hæmorrhage, and it is really to arouse thought about such a complication that this article has been written, for a case of tonsillar hæmorrhage is often allowed to be forgotten as quickly as possible, to spare the feelings of those responsible The following case shows some of these difficulties

A child of 8 was admitted for tonsillectomy The operation was completed quite easily, but three hours later it was obvious that the tonsillar fossæ were bleeding The house surgeon set up a blood transfusion apparatus and gave a pint and a half of blood The bleeding continued, and two hours afterwards the child was sent to the theatre, but did not recover consciousness after the tonsillar fossæ had been tied

The mistake in this case was clearly the decision to give a blood-transfusion rather than to tie the bleeding vessel at once

A boy aged 12 had his tonsils and adenoids removed in the morning, and during the afternoon the house surgeon was called because of bleeding The house surgeon was inexperienced and thought that he could tie the blood vessel in the tonsillar fossa under local anæsthesia He therefore sprayed the throat freely with a 10% solution of cocaine Within half an hour the child died from cocaine poisoning for the cocaine had been absorbed through the raw tonsillar fossæ

The correct treatment for hæmorrhage within twenty four hours is to tie the blood vessel under general The only exception is in the case of a well disciplined adult who may allow local pressure of a sw if he has been given a small injection of morphine fir

A warning should be given against the use of sedativ in these cases, except in small doses Patients who bl after tonsillectomy seem to be unusually sensitive t morphine and the barbiturates, and I have records o two patients who died after tonsillectomy, when n cause could be found except a large dose of sedativ given in each case for slight hæmorrhage

If another operation is needed, the anæsthetist mus be expert, there is a serious risk that blood will b vomited and inhaled during induction of anæsthesia, o that a blood-clot will become dislodged from the tonsil fossa and obstruct the laryngeal orifice I have witnessed both these disasters and the promptness with which my anæsthetist, Dr F H Blackburn, handled them

The detailed method of controlling recurrent hæm rhage differs little from that already described f hæmorrhage during tonsillectomy, except that I have th practice of tying the pillars of the tonsillar fossa, besid tying the blood-vessel to make sure that the bleeding controlled

The bleeding may sometimes come from the pharynx The cause may be a small piece of tissue which has been left behind, or a tear of the wall by the curette If the bleeding has been serious enough need a second anæsthesia, the blood vessel should b sought for and tied, and a gauze pack left in the naso- pharynx for twenty-four hours The pack must b attached to a tape leading out of the mouth so that can be removed

Bleeding from the nasopharynx is fortunately rare

Secondary Hæmorrhage

Hæmorrhage after the first twenty-four hours aft operation is seldom serious, and only once in the last t years have I had to tie a blood vessel for this reason

The cause of bleeding is usually the separation of th slough from the tonsillar fossa, since this may not ta place for ten or twelve days, secondary hæmorrhage ma be delayed for that length of time The chance of hæm rhage can be guessed by the amount of slough in th tonsillar fossa If the slough is large, there is a grea risk of hæmorrhage, a clean tonsillar fossa is likely give no trouble The chance of secondary hæmorrh controls the length of a patient's time in hospital, he is sensible and knows what to do if there is bleeding can be discharged in three days, but our custom is to k an adult in hospital for six days and a child for four da

The treatment of secondary hæmorrhage is simple, it is to keep the patient in bed and to prescribe a sedati such as morphine gr 1/4 The only indications for second operation are a severe and repeated loss of b and a steadily rising pulse rate, both of which are The prevention of secondary hæmorrhage lies in prevention of slough in the tonsillar fossa, and a towards this is strict cleanliness in the operating the-

To complete the risks of tonsillectomy, it is only to report the sequence of events when a swab has left behind Every surgeon has his own method avoiding this mistake, and each method is born of h experience, for few surgeons have not had to remove swab on the day following operation A swab can ea be left in the upper part of the tonsillar fossa, where fortunately remains until it is removed I know of o one case where it was inhaled and caused a lung absc I try to avoid leaving a swab by feeling both fossæ the nasopharynx at the end of the operation, and looking into both fossæ with the help of a headlight

No doubt many of my colleagues will be able to other examples of risks of tonsillectomy, but this should be enough to act as a warning to those who that such a common operation must in time become minor operation

SERUM-CHOLESTEROL LEVELS IN ELDERLY PEOPLE LIVING AT HOME

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IT has been suggested that the serum cholesterol level influenced by age, sex, diet, and metabolic state. uch of the evidence relating the serum-cholesterol level o the presence or absence of certain degenerative con itions, such as arteriosclerosis is contradictory. For ld people only scanty data are available. In the course f a detailed medical survey of old people living in heir own homes the serum-cholesterol levels were etermined and related to age, sex, diet, and various linical conditions.

Methods

election of Group

The final group consisted of 98 men aged 66–85 and 41 women aged 61–87. The sample was drawn in arch 1948 and was a 1:30 random selection from the ood office register of men and women residing in Sheffield who had reached pensionable age (65 in men and 60 in omen). Only those living alone or with spouse were ncluded in the medical survey. Medical students (30 nen and 34 women) aged 18–20 served as controls for the serum-cholesterol determinations.

linical Examination

The old people were medically examined in their homes. Samples of blood were taken by venepuncture; the time of the day at which the blood was taken varied. Ophthalmological examinations were made at the Royal Hospital, Sheffield, by the staff of the ophthalmological department.

Nearly every person examined presented some evidence of clinical abnormality: raised blood pressure, a story of angina, evidence of arteriosclerosis, spontaneous ruising, and chronic ronchitis were very common. It was decided therefore to exclude from the study only those cases in which there was evidence of disordered thyroid function (1 case) or glycosuria (2 cases).

As a criterion of obesity the thickness of a skin fold (the dermis with the underlying panniculus adiposus) was measured on the abdomen at the level of the umbilicus in the lateral plane. The skin fold was picked up with the thumb and forefinger and held in position while the thickness was measured with callipers, which were spring loaded so that all the readings were made under constant pressure.

Radiological examination of the chest for evidence of aortic calcification was carried out at the Royal Hospital, Sheffield, by Dr. J. L. A. Grout.

Dietary Survey

Information was collected on the consumption of food and drink by each old person for a week. A spring balance and standard tablespoons and teaspoons were provided (Widdowson 1936, Beltram and Bransby 1950). The dietary survey was completed satisfactorily by 84 women (59%) and 71 men (72%).

Serum-cholesterol Determination

To 20 ml. of a mixture of acetone and absolute alcohol (equal parts by volume) 1 ml. of serum was added slowly with shaking, the total volume was made up to 25 ml with the above mixture and the flask was stoppered, shaken, and allowed to stand overnight. Next morning after further shaking the mixture was centrifuged; 5 ml of the supernatant fluid was evaporated to dryness, the dry residue was redissolved in 5 ml. of chloroform and the tube was stoppered and placed in a waterbath at 20°C for several minutes. 3 ml of a fresh acetic anhydride-sulphuric-acid mixture (10:1 by volume) was then added, the tube was restoppered, the contents were mixed, and the tube was placed in a waterbath at *exactly 20°C in the dark for precisely 20 minutes*. The optical density was then read photo-electrically with an Ilford no. 204 (Tricolour Red) filter. A standard solution of cholesterol in chloroform was taken through the later stages in parallel with each batch of tests.

The serum cholesterol levels were also determined by the same method but using Bloor's original method of extraction (Bloor 1916). Others were determined by substituting for the acetone-absolute alcohol mixture a mixture of ether and absolute alcohol (1 part to 3 parts by volume).

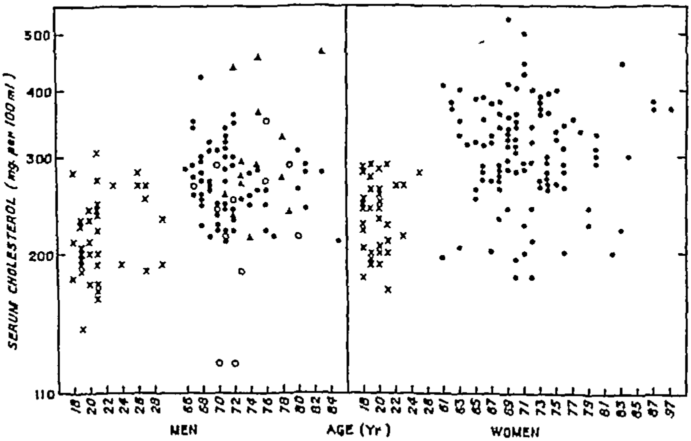

Fig 1—Relation between age and serum-cholesterol level:

○ HEAVY DRINKERS
× CONTROLS
▲ TEETOTALLERS
● OTHERS

TABLE I—RELATION BETWEEN (LOGARITHMIC) MEAN SERUM-CHOLESTEROL LEVEL AND SEX

—	Old people		Controls	
	Men	Women	Men	Women
No of cases	98	141	36	34
Logarithmic mean serum-cholesterol level	2 4277	2 4915	2 3234	2 3680
Standard error of difference	0 0153		0 0174	
t	4 18		2 57	
P	Less than 1%		Between 1% and 2%	
Logarithmic mean serum-cholesterol level (mg per 100 ml)	268	310	211	233

Results

Methods

Comparisons were made between the three different methods of extraction by applying more than one method to the same serum In studies of 53 sera no statistically significant differences were found between the results yielded by the different methods of extraction

Age and Sex

The serum cholesterol values for all the old people were plotted as a frequency distribution for each sex and were skew, plotted on semi-log paper they appeared to be lognormal This was confirmed by the calculation of Fisher's g_1 The numbers in the control groups were insufficient to establish the type of distribution, we have assumed the distribution to be lognormal There is evidence from the work of Wootton, King, and Smith (1951) that the distribution of whole-blood cholesterol level in the age group 18–50 follows a lognormal distribution For these reasons the logarithms of the serum-cholesterol values have been used for all the calculations, in all the diagrams a logarithmic scale has been used for the serum-cholesterol values The relation between cholesterol value and age for both the old people and the controls is shown in fig 1

There is a significant difference between sexes both in the old people and in the controls (table I), women having, on the average, a higher serum cholesterol level than men of the same age In both sexes there is a significantly higher serum cholesterol level in the old people than in the controls (table II) The serum cholesterol level is lower in subjects over the age of 70 Analysis of variance shows that the differences are not significant at the 5% level

The subjects investigated may be regarded as a representative group of old people aged over 60, and the serum cholesterol results provide limits for "normal" values If the normal range be regarded as the mean of the logarithmic values plus or minus twice its standard deviation, the results reconverted into milligrammes of cholesterol per 100 ml of serum yield the following values for people over 60

Men mean 268 range 176–409
Women mean 310, range 200–481

Another method for the presentation of normal range has been suggested by Wootton et al (1951) The outer or 1% limits enclose 98% of results and the inner or

TABLE II—AGE DIFFERENCES IN SERUM CHOLESTEROL LEVELS

—	Men		Women	
	Controls	Aged	Controls	Aged
No of cases	36	98	34	141
Logarithmic mean serum-cholesterol level	2 3234	2 4277	2 3680	2 4915
Standard error of difference	0 0178		0 0160	
t	6 02		7 45	
P	Less than 1%		Less than 1%	

10% limits enclose 80% of the resu
that individual results falling outsid
should be viewed with suspicion,
outside the 1% may be considered
limits based on our results are shown

Intake of Fat

In 64% of the cases studied an
survey was made The mean daily in
range of values in grammes for each se

Men mean 85 7, range 44 5–138 1
Women mean 72 2, range 32 5–142 6

In the men there was no significant c
the intake of fat and the serum ch
cases, $r=+0\ 102$, $P>10\%$), whereas
significance of the correlation was be
3% levels of probability (84 cases, r
bination of the results for the two sexe
coefficient which was statistically s
the 1% and 2% levels of probabili
+0 184)

Alcohol

Information was available about t
alcohol by some of the men The r
into 12 heavy drinkers, 14 lifelong t
others To be eligible for classification
a history of drinking five pints or
throughout most of life was required
made of the mean serum cholesterol le
drinkers (224 mg per 100 ml) with
teetotallers (305 mg per ml) The
the difference was significant betwee
levels of probability ($t=2\ 70$) The va
drinkers and the lifelong teetotallers a
fig 1

Obesity

The relation between the serum-ch
the body-weight was studied by m
diagram There appeared to be an u

TABLF III—UPPER AND LOWER LIMITS OF
LEVELS IN OLD PEOPL

—	Lower limits (mg per 100 ml)	
	1%	10%
Men	130	220
Women	185	230

high serum cholesterol levels in the h
the correlation coefficient between the
levels and the body-weights was
significant

Fig 2 shows the thickness of the
abdomen and the corresponding seru
in the older subjects In the men there
correlation between abdominal skin-f
serum cholesterol level (93 cases, $r=+$
9%), in the women the correlatio
between the 1% and 2% levels of prob
$r=+0\ 2180$) When the correlation
two sexes were combined, the result
significant between the 0 1% and 0 5%
(225 cases, $r=+0\ 1974$)

Manifestations of Conditions Possibly Atherosclerosis

25 men and 38 women gave a history
of effort 3 men had experienced at
diagnosed as cerebral thrombosis, 9

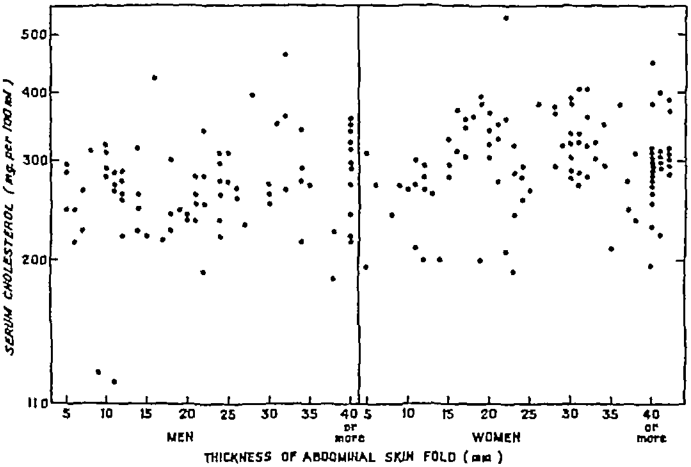

Fig 2—Relation between obesity (measured by thickness of abdominal skin fold) and serum-cholesterol level in 93 old men and 132 old women

lateral radiographs as having calcification of the aorta and 30 men and 37 women showed depressed crossings of the retinal blood vessels. It was impossible to establish any statistically significant relation between the serum cholesterol level and the presence or absence of any of these conditions.

Blood pressure

Scatter diagrams showing the relation between the serum-cholesterol level and the systolic and diastolic blood pressures did not show any correlation.

Eye Changes Associated with Ageing

In 175 of the subjects (78 men and 97 women) the eyes were examined 31 men and 23 women showed well marked arcus senilis 2 men and 5 women had senile atrophy of the retina; and 19 men and 35 women had senile cataract No significant relation was found between the serum-cholesterol level and the presence or absence of these conditions.

Discussion

The blood specimens were taken at various times of the day irrespective of meals and rest periods. Ordinary meals are known to have little effect on the serum cholesterol level. Keys et al (1950) found no difference between the serum-cholesterol levels of specimens taken under basal and non basal conditions although Groen et al. (1951) found that infections, trauma severe exercise and emotional tension could affect the serum cholesterol level.

Some modifications were introduced into the Bloor (1916) technique for determining serum-cholesterol levels. Extraction of the lipoids with a cold acetone alcohol mixture overnight appeared to give results comparable to those given by extraction with an ether alcohol mixture and with greater safety from fire and peroxide explosions Sperry and Brand (1943) discussed the need for careful control of the temperature and of the time allowed for colour development in the Liebermann Burchardt reaction. D.A Podmore (personal communication) found that the greatest development of colour was obtained by using 55 parts of cholesterol solution in chloroform 30 parts of acetic anhydride, and 3 parts of concentrated sulphuric acid Free cholesterol gives less colour than does the equivalent amount of cholesterol in ester form and the Liebermann Burchardt reaction applied directly to an extract of serum gives higher results than those obtained if colour development took place after hydrolysis of the ester (Gardner and Williams 1921 Reinhold 1936 Sperry and Brand 1943, Kibrick et al 1951) Keys et al (1950) found this difference to be 2 1 mg per 100 ml but did not give full details of their technique Reinhold (1936) and Podmore (personal communication) have shown that the difference depends on the conditions under which the colour is developed the important factors being the temperature the proportions of the reagents, and the time allowed for development of the colour

The results show that the elderly women had a higher serum-cholesterol level than men of the same age The finding of a higher serum-cholesterol level in the old people compared with the young people is in general agreement with the findings of Barker (1939) Kornerup (1950) and Keys et al (1950) in men and of Mühlbock and Kaufmann (1938) and Gram and Leverton (1949) in women Sperry and Webb (1950) found that in 12 people (6 men and 6 women) the serum-cholesterol level had risen 15–30% after about fourteen years and in 10 people (8 men and 2 women) the same interval of time had produced no significant change the age ranges for these subjects at the end of the experiment were 38–57 for the men and 35–54 for the women Page et al (1935) studied the serum-cholesterol level of 67 men aged 21–101 and claimed that there was no significant change with increasing age but the regression line for the data of Page and his colleagues between the ages of 21 and 79 calculated by Gertler et al (1950) showed a rise of the serum-cholesterol with age which was significant on the 5% level. Barker (1939) suggested, and Keys et al (1950) found that with the onset of old age in men the serum-cholesterol level began to fall; the present study does not contradict such a finding in both men and women. If the higher serum-cholesterol levels were associated with lessened expectation of life after middle age, there would be a selective removal of those persons with the higher values, which would lead to a fall in the mean serum-cholesterol level in the older age groups

Hildreth et al (1951) and Keys (1952) have shown that extreme variation in the intake of fat changes the serum cholesterol level Groen et al. (1951) have shown that variations in the cholesterol content of the diet between 1 5 mg and 900 mg per day can cause variations in the serum-cholesterol level Gardner and Gainsborough (1928) found a similar effect The range of dietary intake of fat was greater in the women than in the men and this may explain the apparent correlation between the serum-cholesterol level and the intake of fat in the women but not in the men We also found an over all correlation when the two sexes were taken together These results indicate that even the variations in intake of fat on normal diet may be sufficient to alter the serum cholesterol level

The finding of a relation between the intake of alcohol and the serum-cholesterol level is difficult to comment on Wilens (1947c) expressed the opinion that the lower incidence of atherosclerosis observed in alcoholics compared with non-alcoholics was the result not of alcoholism but of associated differences in age, blood-pressure, and nutrition, to these might be added race and diet Some of these factors may well be involved in the relation between alcoholism and the serum cholesterol level

There was no statistically significant relation between body-weight and serum cholesterol level, but weight alone is not a true measure of obesity Keys (1949) has found a better measurement in the thickness of an abdominal skin fold, his results indicated that fatter men tended to have higher serum cholesterol levels These differences analysed by the only statistical methods open to us were not significant, but possibly a more refined technique would have demonstrated a significant difference The analysis of our data suggests that there is a relationship Such a finding is of considerable interest because a high incidence of atherosclerotic complications in the obese is a well-known experience of life-assurance companies, and Wilens (1947a and b) found that severe atherosclerosis is ten times commoner in fat people than in thin In experiments on animals Firstbrook (1951) found that the greater the degree of hypercholesterolæmia the more rapidly did atherosclerosis develop, and that the atheromatous condition developed more slowly in thin animals than in fat There is strong evidence that in man also atheromatous conditions are commoner with a high serum cholesterol level (Gubner and Ungerleider 1949, Duff and McMillan 1951, Katz 1952) We were unable to demonstrate any relation between the serum-cholesterol level and manifestations of atherosclerosis

Our results did not show a significant association between the serum cholesterol level and the blood-pressure

No relation appeared to exist between the serum-cholesterol level and the presence or absence of arcus senilis or of senile cataract, the number of cases of senile atrophy of the retina was too small for any reliable conclusion to be drawn Garn and Gertler (1950), in their survey of Aleutian islanders, found that the serum-cholesterol level was no higher in those with well marked arcus senilis than in those without

Summary

The mean serum-cholesterol levels in elderly men and women living at home were significantly higher than in control groups of younger people

For both the young and the old the mean serum cholesterol levels in the women were significantly higher than in the men

The mean serum cholesterol level tended to decrease after the age of 70

The normal range for the serum cholesterol level determined by the technique described was

Men aged 60–85 176–409 mg per 100 ml
Women aged 61–87 200–481 mg per 100 ml

There was a significant correlation between the dietary intake of fat and the serum-cholesterol level in the women but not in the men The combined results for the two sexes gave a significant correlation

Lifelong teetotallers had, on the average, a significantly higher serum cholesterol level than had heavy drinkers

There was a significant correlation between the thickness of an abdominal skin fold and the serum cholesterol level in the women but not in the men The combined results for the two sexes gave a highly significant correlation

No relation could be established between, on the one hand, the serum cholesterol level and, on the other hand, intermittent claudication, angina, cerebral thrombosis, aortic calcification, depressed crossing of retinal blood-vessels, arcus senilis, senile atrophy of the retina, and cataract, or the height of the blood-pressure

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THE INSULIN MYTH

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The outstanding importance of schizophrenia as a biological and social problem makes the critical evaluation of its treatment a matter of the first interest and no mere parochial concern for psychiatrists In this paper I shall try to show that there is no sound basis for the general opinion (as stated, for example, in a refresher course by Sargant and Slater in 1951) that insulin-coma therapy counteracts the schizophrenic process in some specific manner, and that its therapeutic effects are greatly superior to those obtainable by electro-convulsant therapy (E C T)

A treatment for schizophrenia may be evaluated by its immediate and remote effects on (1) early cases in which spontaneous remissions make the value of any therapeutic procedure formidably difficult to assess, (2) dilapidated chronic cases in which the extreme unlikelihood of spontaneous improvements makes even small groups of decidedly positive results significant, and (3) individual cases observed over long periods with repeated administration of the treatment

The Early Case

It was soon recognised that useful results with insulin coma were unobtainable after two or three years of uninterrupted psychosis and the popularity of the thod depends entirely on its supposed value in recent es. Usually, in the accounts of its application eries of patients treated by insulin coma is compared ıer with a series treated in the pre-shock era or with parallel untreated or E.C.T treated, series. These allel series, though seldom comparable in more ın a few respects, are often regarded as true controls. reover where the series compared do include cases longer standing no distinction is made between those continuous and those of intermittent psychosis The ole method is riddled with sources of fallacy deriving m the nature of the disease, and from the nature of ulin treatment itself.

llacies Arising From the Nature of Early Schizophrenia

l The diagnostic criteria are highly subjective and riable and certainly very different from what they re in the past, when recovery implied misdiagnosis nd and Bruceland (1937) in a study of all patients mitted to a Philadelphia mental hospital in 1927–28 ınd that of 116 cases finally labelled schizophrenic er five years, only 10% had recovered and 31% had overed or improved but if the early diagnosis s accepted, the rates for schizophrenia rose to 20% overed and 40% recovered or improved. Nowadays ulin coma is often begun on a suspicion, perhaps lstered by a Rorschach or other test and almost reports fail to specify the diagnostic determinants d their distribution The increased readiness to gnose schizophrenia in favourable cases is reflected Malzberg s (1943b) finding that, in New York State, e incidence of schizophrenia and the discharge rate e both rising

2 Halliday (1946) has traced the profound changes the quality *and relative incidence of psychogenic* nesses over the past 70 years, and it is quite likely at the schizophrenic psychoses have been affected. deed the great changes emphasised by him in the rly environment of the infant whose experiences are pecially prominent in the psychopathology of schizo renia, are particularly suggestive. As a result it ay well be that the basic prognosis and diagnostic iteria have been altering in such a way as to invalidate e direct comparison of contemporary results with ose of the pre-insulin era

The immediate prognosis of present-day untreated rly schizophrenia is altogether problematic but the llowing summary of a series of 376 schizophrenic ldiers, 186 of whom I followed up by letter two years ter may suggest that acute schizophrenic illnesses e becoming more benign Of the 376 84% were dis arged, nearly all within nine months, as recovered improved sufficiently not to need further hospital re, and the *follow up indicated no strikingly extensive* rapid relapse-rate For 156 cases treated with C T the corresponding figure was 83% of 15 treated th insulin coma, with or without E.C.T., 9 resumed dinary life while for 205 untreated cases the figure s 88% It should be added that in both treated oups a substantial number of psychoses subsided long ter the treatment could have been responsible

It is possible, therefore, that apart from the increasing tection of earlier and milder cases, the scales are ing deceptively tipped in favour of insulin by some ange in the short-term prognosis

3. The influence of nuances of environment on the urse of schizophrenia involves so many imponderables hich cannot be isolated or controlled that to compare sults at different times or places may be quite invalid. uite apart from any theoretical arguments in favour of organic pathogenesis or predisposition for schizo- renia environmental factors have an overwhelming actical significance—as is shown by its changed inci ence in European and African stocks transplanted to e United States of America (Malzberg 1940, Carothers 1947) The importance for the outcome, of environment during treatment was stressed long ago and can be seen in gross form by contrasting the dereliction of chronic schizophrenics in backward institutions with their appearance in hospitals promoting liberty and social life Clearly it is impossible to control, and mistaken to dis regard the less obvious but equally influential variables affecting the response of the schizophrenic to treatment: the very same attendants will change in personality over the years and the transitory junior nurse and doctor the other patients, or even the weather may all conceivably exert a decisive twist Kalinowsky and Worthing (1943) obtained very different results with E C T given in the same way at the same time to schizophrenics in two different hospitals.

Thus inherent in this disease and in the therapeutic environment, are numberless uncontrollable factors which taken together render it insurmountably difficult to validate any method of treatment by simple comparisons of results in early cases in different decades or places, or by different workers—unless possibly a near 100% recovery rate were in question which arises neither with insulin nor convulsion therapies.

Fallacies Arising from the Nature of the Therapy

1 Insulin coma produces drastic modifications in the subject s environment which may well favour improvement in a non-specific manner Insulin patients tend to be an élite group sharing common perils and privileges, they receive an extra diet, are anxiously watched day and night and have concentrated individual nursing for a five hour daily treatment period over two or three months, as well as the attention of a doctor for three of these hours In most mental hospitals they are given, at *a conservative estimate 50–100 times as much medical* and nursing care, measured by the clock, as the general run of non insulin treated patients. A relevant observa tion by Rubé (1948) records a decline in remission rate of schizophrenia with sulphosine therapy in a Paris hospital, from 35–40% in 1932 to 15–20% in 1939 as the novelty of the method and the staff's initial enthu siasm wore off and he suspects a similar development in insulin clinics as routine replaces drama. Cossa et al (1948), recording just such a change, wonder naïvely whether their post war insulin lacks some non hypo glycæmic factor

Few mental hospitals, even today, are able to offer recently admitted patients (let alone schizophrenics who have been in longer than a few months), much more than custodianship rug making the cinema and a chat every week or two with the doctor Inducing two or three electric convulsions a week hardly alters this setting to an extent comparable with the insulin-coma régime—*a fact to be remembered when assessing results.*

2 The mode of selection of cases for insulin coma is biased Reports are uniform that the best results are obtained where without any treatment, the prognosis would be most favourable so except in the unusual circumstances of it being freely available for all cases selected for treatment are only those considered most likely to benefit—that is to say, to get better anyway It is no wonder that an impression" is so often met that the quality of remission after insulin is superior It would be surprising if it were otherwise Practically all reports comparing insulin favourably with E.C T omit to say how patients were chosen for either treatment; but they contain details from which this bias can be strongly suspected.

3 The concomitant administration of E.C T., so often reported obscures even more the specific action if any of the insulin coma itself Induced convulsions are in fact now so often casually mentioned as an ingredient of the coma technique that it cannot be assumed with certainty that recent publications on insulin may not just as well be taken to mean results with E C T

4 Improvements in patients treated with insulin or E C T cannot be attributed simply to the method unless they occur within some limited time, but most reports ignore this Alexander (1944) believes the picture would be much less favourable if improvements appearing more than thirty days after treatment were excluded

The Fallacies Avoided?

Altogether, the evaluation of insulin coma in early schizophrenia presents extraordinary difficulties deriving from both the nature of the disease and the nature of the treatment, and attempts to by-pass the pitfalls are few

Lipschutz et al (1939) designed an experiment to compare insulin with saline injections, both with and without "intensive resocialisation," to assess the relative importance of insulin, of coma, and of extra attention for the outcome But as they treated fewer than 30 cases, only 5 of whom received saline, and only 7 of whom were denied "resocialisation," the positive conclusions reached do not seem justified

Sillman and Terrence (1943) gave 112 schizophrenics daily nitrogen inhalations for one to three months to produce coma and extensor spasms, and some 20% remitted They contrast this with 52% improvements in 62 of the "nitrogen failures" subsequently given insulin coma, E C T, or both, and deduce that the benefits of shock therapies cannot be explained by special attention, fear of death, anoxia, and so forth They give no clinical details, no reason for only 62 of the failures receiving shock treatment, and no account of what became of the rest, so that it is not conclusive that the nitrogen and other results differ significantly

Can all the difficulties be overcome? Penrose and Marr (1943), when assessing shock therapies in Ontario State hospitals, devised an ingenious method for eliminating variability in diagnosis, symptomatology, and estimation of improvement They constructed tables (like life assurance tables) to enable comparison of the number of treated patients remaining in hospital on any given date with the number to be expected without treatment, based on a control method by sex, age on first admission, and lapse of time since first admission, but not by diagnosis, since (as they illustrate) certain diagnoses predominate completely at particular age ranges From this, they confirmed that over a period of two to three years, the shock treatments produced definite benefits in affective psychoses but almost none in 1041 patients diagnosed as schizophrenic, and in these, if there was any benefit at all, it was with convulsion therapy rather than insulin

INSULIN COMA VERSUS E C T

Being concerned here only to expose a myth, I shall not deal with E C T technique in schizophrenia, except to mention that its casual administration without formulated principles is a waste of time

Favourable accounts usually appeal for adequate dosage, and the course recommended, for instance, in a popular British textbook (Sargant and Slater 1947) is altogether insufficient Danziger and Kindwall (1946) calculate statistically that 26 convulsions is the minimal course, whereas Kalinowsky and Worthing (1943)—when describing in 200 cases results as good as those quoted as the best obtainable with insulin by Kalinowsky and Hoch (1946) in their standard book—insist on 20 Their diminished success in another hospital for voluntary patients, and also the poorer prognosis of their less florid cases, show how easily simple comparisons may mislead However, Hamilton and Wall (1948) report 100 such cases 67% of whom were at home, 43% recovered between eighteen months and six years after E C T, this result contrasts favourably with their experience of ten years before (though this contrast, as already explained, may have more than one interpretation) Strong evidence of the benefits of convulsion therapy is contained in Dedichen's (1946) statistical analysis of shock treatment in all Norwegian mental hospitals The few insulin treated cases briefly presented disclose incidentally that of 128 "pure" schizophrenics ill more than a year only 5 remitted

Of the innumerable reports on insulin-coma thera only some of the best known, careful, and typical ca be considered here, since the vast majority are mo tonously illustrative of the fallacies listed above Th by Ross and Malzberg and others, appearing since 1 on its use in the 19 New York State hospitals, ha undoubtedly had most influence in promoting its These cover 1039 insulin-treated, 1140 leptazol-conv sion-treated, and 1039 untreated controls, but distribution of diagnostic and symptomatic data w might show the groups to be comparable are not gi and there is much internal evidence to suggest, in that they are not comparable Some occurred in 65% of the insulin group (varying in hospitals from 35 to 91%), but in only 26% of controls, this, for an unselected sample, is low Improvement was seen in only 35% of the group which again seems surprisingly low until a tion from their tables reveals that only 15% of been ill for less than a year Also the number of c sions in each case is not given There are some anomalies Thus the control group's mortality (4%) greater than that in the insulin series The recovery (1 6%) in the leptazol series was under half that of controls, and the "much improved" rate (9·9%) also less—findings which show that the groups have been selected at random and were not prog similar In fact, a later account by Malzberg (1943 E C T in the same hospitals gives results 3–4 times than in the original convulsion-treated series. Also is evident from the two-year follow up report some insulin-treated cases received leptazol—how is not stated Finally, a 1944 report on insulin from the same hospital group shows a 58% discharge-rate untreated cases (Temporary Commission on Hospital Problems 1944), which deprives the improvement in the original controls of any meaning

Danziger and Kindwall (1946) find that, per 100 sions, the expectation of recovery in the "most able three months" is 1 5 for untreated 34 for E C T -treated, and 45 for insulin treated, less of duration of illness"

Before accepting the apparent superiority of insulin it be noted that (though clinical details are not given) 78% their 83 insulin patients had been ill for less than two compared with 63% of the 205 E C T cases thus there ably was some mode of selection, not specified, fo treatment Secondly, E C T was only given twice sometimes with interruptions, and petits mals were co as treatments Again, they take their figures for untreated category from discharge rate tables for all State hospitals in 1933—a comparison which has snare mentioned including different criteria of recovery diagnosis, and length of illness on admission Even tables, however, indicate that at three years the dis rate has risen to 32 6%—which can stand quite res beside results three years after insulin treatment At the results of these workers show a hastening of recov but they do not hesitate to ascribe this specifically to insulin coma rather than to the non specific treatment tion, since, they claim that treated patients had "no (except during actual treatment) not given to other pat and not ordinarily given in public institutions. therapy was of the most casual and superficial type

Insulin is strongly favoured by Linford Rees (1 in a widely quoted British study He compares E C T, and electronarcosis (E N) by the immediate come and follow-up of 208 courses of treatment in "experimental population" of 160 schizophrenics assessed separately the 97 insulin, 72 E C T, and 39 courses, so several cases find a place in more than group

In a wide range of features the groups corresponded, whether these were 160 consecutive schizophrenic admis over a period or whether they were somehow chosen fr larger population is not clear In the absence of infor about dosage, it may be surmised, from the poor results eir similarity in cases with poor or good prognosis, that E.C.T as inadequate by the standards quoted above Also there o some odd numerical discrepancies Thus in 18 patients all ree treatments failed accounting thus for 54 of the 208 ourses, and leaving only 154 courses for the other 142 patients that 12 at most of these could have had two treatment urses. Yet it is stated that 21 recovered with insulin after ilure with E.C.T or E.N When the percentages on which bases his conclusions are reconverted into whole numbers, any of the conclusions seem doubtful. The relapse-rate ter recovery is 7% with insulin in contrast to 33% with N ; but conviction melts when the E.N recoveries are seen number 3 in all The percentages demonstrating the periority of insulin in prognostically favourable cases refer a mere dozen or less in each group

Nielsen et al. (1942) described 316 schizophrenics each eated with 40 insulin comas and 10 convulsions and bitrarily selecting 100 of them by admission dates, ey compared them with 100 controls similarly chosen om admissions between 1931 and 1937, matching in ge and duration of illness They found no evidence of nefit in the treated group

LATE EFFECTS

Of the more remote effects of insulin some background provided by Blair's (1940) review of published work the prognosis of schizophrenia ' An average of 40% cases admitted to mental hospitals recover or prove .. relapses occur in about 20% of the cases scharged as recovered or improved of which approxi ately half are permanent."

In Ross and Malzberg's two year follow up 45% still owed some improvement 27% being recovered or much proved Bond and Rivers (1942) report a recovered or much improved rate of 55% at the end of treatment fall g to 31% in three years This three-year rate was still ice as high as the rate in 1937 at the same hospital; but en if the contrast were valid, the influence specifically of sulin would remain uncertain. Gralnick (1946) compares C.T in 208 with insulin in 158 schizophrenics and finds in vour of insulin, though, like others, he fails to give details method of selection for either treatment ages duration of ness in each group clinical features, or relapse rates. In a rvey (1945) of seven years experience with insulin in 554 ses, he finds that half the total on parole are back in hospital tween the fourth and sixth year and after six years, 73% back. He observes that the results bear no relation to the mber or duration of comas and infers that it is the insulin atment situation which matters It is noteworthy that eudenberg (1947) who gave E.C.T where there was no sponse after 20 comas, goes on to insist on prolonged courses insulin treatment for better results.

Rennie (1943) of Johns Hopkins considers that in a odern private institution the results are little different th and without insulin Similarly Gottlieb and Huston 943) found no significant difference at the end of four ars in two groups of schizophrenics, 66 insulin treated d 132 having only some psychotherapy They state at the groups were clinically alike but do not mention ndom selection Indeed this seems to be an endemic ficiency in insulin studies.

In a later contribution (1951) 128 cases having brief psycho rapy with defined aims are compared with 65 receiving insulin comas and 143 having E.C.T ; the groups were milar but for a slight excess of catatonics having E.C.T er four years, no important differences in results were at y time discernible and none emerged even when early ses of acute onset were studied separately

Libertson (1941) relating experience since 1937 with insulin one hospital compared 165 cases with a—prognostically—st unfavourable control group admitted simultaneously was astonished to discover no difference in results by 1941 d a close resemblance in 50 insulin and 41 controls with less an six months illness.

Roberts (1942) compared 74 male patients 46 of whom had nvulsion as well as insulin-coma therapy with untreated ntrols matched for age duration, and diagnostic category d observed no difference in outcome after two years, though transient improvements were 2 75 times commoner in the treated group.

Palmer et al (1950) present a very discouraging survey of 303 schizophrenics at one hospital Of 182 insulin treated patients who had not previously received E.C.T only 34% were discharged, while between eighteen months and six years later only 20% were still out of hospital and only 6% really well Of 183 who had not responded to E.C.T only 17 8% were discharged; and of 100 patients who did not respond to insulin, 15% were discharged after E.C.T Insulin courses were of 50 comas, and they had 2 deaths The E.C.T dosage is not stated.

In the light of the evidence so far presented, and apart from other considerations set out below it is clear that the justification is slender indeed for the way in which money and staff are expended on clinics for insulin coma Insulin offers the schizophrenic no long term benefits at best it hastens improvements that would occur anyhow with simple care in hospital, and which could be accelerated at least as well with E.C.T and there is no evidence that this uncertain benefit is attributable to the insulin itself and not to the insulin treatment situation. If the latter is the operative factor, its effects could surely be reproduced by some more rational and less hazardous means.

The Chronic Case

The extraordinarily few accounts of the use of insulin coma in long-standing schizophrenia all date from the early years of its use, when occasional cases of several years duration also appear as failures scattered in other reports.

Rossman and Cline (1938) claimed that of 52 cases ill an average of over four years, 83% improved 40% being recovered or much improved, but this contradicts all subsequent opinion, and indeed, if reproducible should have reduced the mental hospital population markedly Barker (1939) treated 10 Negro men who had been ill for an average of seven years (but whether continuously or in hospital is not stated) and of 13 completing the course 4 were ill less than three years, 1 died, 3 improved, and 4 left hospital; he draws conclusions by converting these figures into percentages. Fröshaug and Thomstad (1938) treated 32 women with an average of eight years psychosis The single case with " full remission was ill less than two years; 4 cases had ' good remissions " but none could leave hospital and one certainly remained hallucinated, the effect being, chiefly quieter and cleaner behaviour 6 showed partial remission with even less benefit and there were 10 instances of some transitory reductions of symptoms lasting a few days or weeks.

The general view is thus justified that insulin has no place in chronic schizophrenia but there is ample evidence that E.C.T can set off profound, if incomplete restorative changes in this most stagnant of conditions.

Moore (1943) selected 37 chronic schizophrenics of an average nine years standing all severe behaviour and nursing problems, and gave them thrice-weekly E.C.T for two to three weeks, followed by maintenance dosage and in 26 there was no question about the value of continuing the treatment —they became sociable and employable while appetite, sleep and faulty habits were almost uniformly controlled. Shoor and Adams (1950) relate that during three months intensive trial of E.C.T in the most refractory female ward of a mental hospital, the character of the ward changed radically from that of a chronic disturbed ward to that of a quiet chronic ward with a 90% reduction in sedation and restraint. Fergus (1952) gives an excellent account of what can be achieved with E.C.T in chronic schizophrenia.

Clearly the longer the psychosis endures unfluctuating over the years, and spontaneous recovery or chance improvements with treatment become less likely the probability grows that E.C.T counters the disease process in some specific way while the therapeutic activity of insulin and its superiority to induced convulsions become still more clearly mythical. Yet, nowadays, when E.C.T can bring about improvements that would have been astounding fifteen years ago in wards with schizophrenics in their most chronic state, a widespread apathy exists about its possibilities in these and in recoverable cases

The Individual Case

Perspective in the treatment of schizophrenia requires appreciation of its natural course in terms of long spans of time It may occur as single or widely separated episodes without sequelæ, or as recurring episodes with residual damage, sometimes finally amounting to gross personality destruction, or it may never remit after the first manifestation Often it is impossible to decide which of these developments is taking place and so, where some somatic interference is attempted therapeutically, repeated response acquires a significance that an isolated ensuing remission cannot have It is often asserted that schizophrenics that have recovered after insulin coma should be treated again if they relapse, but anything beyond the scantiest experience to bear this out is not on record With convulsion therapy on the other hand, relapse after withdrawal, and repeated improvement, are commonly seen in all phases I hope in due course to publish studies showing that the schizophrenic patient may be as dependent on E C T for a normal existence as a diabetic is on insulin

Summary

Schizophrenia presents a major medical and social problem, and the widespread belief in the indispensable value of insulin treatment is a matter of general concern

The difficulties of assessing any treatment in schizophrenia, and in particular, insulin coma, are discussed

In face of these, the evidence for the value of insulin treatment is unconvincing From the point of view, in turn, of the early case, the chronic case, and individual case studies, there is no proof of any specific therapeutic effect, and the long term prognosis is in no way influenced

Insulin certainly offers the schizophrenic no more benefit, and perhaps considerably less, than does E C T

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PATENT VITELLO-INTESTINAL DUCT WITH ASSOCIATED FISTULA AND PROLAPSE

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It has been estimated that congenital abnormalit of the vitello-intestinal duct occur in 1–2% of peo (Brennemann 1948) A review of 144 cases in which t whole length of the persistent duct was patent show that of the 132 cases in which the outcome was k 46 (35%) were fatal, of 30 cases complicated by pr of the small intestine through the umbilical fistula (87%) were fatal, even in the cases without this gr complication the mortality was 20%, and the ra of males to females was about 5 or 6 to 1 (Scalettar et

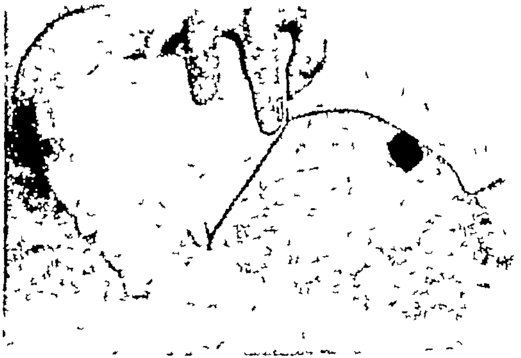


Fig 1—Raspberry-like tumour at navel

1952) Garrett (1918) reported the abnormality homozygous female twins

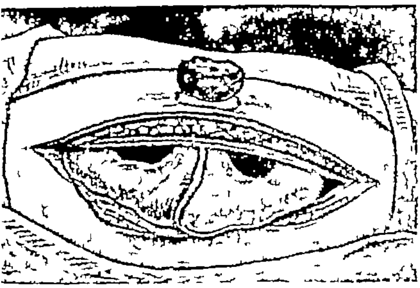
EMBRYOLOGY

In early embryonic life portions of the yolk-sa included in the embryo to form three separate part the intestinal tract foregut, mid gut, and hind The connection between the mid gut and the yolk proper becomes constricted and drawn out to form vitello-intestinal duct At about the fifth month fœtal life this duct is cut off from the mid gut, exceptionally it may remain patent as a constituent the umbilical cord, or its proximal part may persist in about 2% of people, as Meckel's diverticulum. the duct is normally obliterated, that part of the that runs in the wall of the duct disappears also, proximal part persists as the superior mesenteric

CASE-REPORT

In the following case, successfully treated by the vitello-intestinal duct persisted after birth lumen patent and its distal mucosa prolapsed, fo "raspberry" tumour or enteroteratoma The intestinal artery was represented by a fibrous cord

A male infant was delivered at full term on Jan. 30, There was no history of maternal illness in early p which was uncomplicated throughout The baby 7 lb 1 oz at birth and had a healthy brother aged 3 There was no history of congenital defect in any



g. 2—Structures found at operation : patent vitello-intestinal duct and remains of vitelline artery

e family The neonatal period was unusual in that the nbilical cord did not separate until the fourteenth day, aving a bright-red nodule which, in the next day or two creased in size to nearly 1 in in diameter There was a ttle serous and mucous discharge from the surface of the ass but meconium or fæces were never seen. There was no owel or urinary disturbance The baby was admitted to the ediatric department of this hospital at the age of 18 days.

Examination—His general condition was good The mbilical area showed a red raspberry like mass about $^{3}/_{4}$ in diameter (fig 1). The size of this tumour varied from in. to nearly 2 in. in diameter sometimes from day to day ccording to the amount of prolapsed intestinal mucosa A nall dimple-like depression could be discerned in its centre nd a probe passed into it revealed a patent duct leading down nto the gut Lipiodol 10 ml. injected into this dimple was hown radiographically to pass into the lower ileum and, wenty four hours later into the colon A patent vitello ntestinal duct with raspberry tumour (enteroteratoma) was iagnosed.

Operation.—As after a period of observation, there was no ecal discharge or obstructive symptom and the child was riving it was decided to postpone operation. He was admitted at the age of 6 months. The tumour was rger but, apart from this, he was healthy The operation as done under ether and oxygen anæsthesia. The abdomen as entered through a right paramedian incision with its ntre at the level of the umbilicus. A thin walled track in. in diameter stretched from the umbilicus to the ileum $^{1}/_{2}$ in. from the ileocæcal valve. To the right of this was a un fibrous cord stretching from the umbilicus to the ileal esentery close to its junction with the mesenteric border of e bowel (fig 2) This cord, the remains of the vitelline rtery though lying in close apposition to the peritoneal urface of the patent duct was nevertheless quite separate om it and thus formed a highly dangerous potential cause of ternal strangulation, because a loop of bowel could easily ip between the duct and the cord It was excised together with the vitelline duct The vitelline duct was divided about 1 cm from the ileum and inverted with two layers of fine catgut without narrowing the bowel lumen The remainder of the duct with the umbilicus was excised through a circum umbilical incision. The vertical incision was closed in layers and the umbilical defect repaired with the fashioning of a new umbilicus (fig 3)

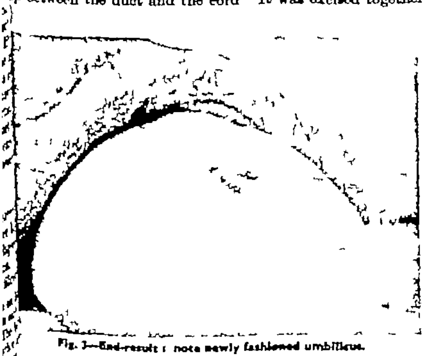


Fig. 3—End-result : note newly fashioned umbilicus.

Convalescence was uneventful, except for some pyrexia and mild infection of the umbilical wound. The baby took food normally within a few hours of the operation and showed no sign of peritonism or other untoward intra-abdominal disturbance and on the second day after operation a normal motion was passed

Follow-up—The baby was brought for inspection a month after the operation and again three months afterwards *He is in excellent health and thriving*

Pathology—The operation specimen consisted of a disc shaped tumour $^{7}/_{8}$ in in diameter and $^{3}/_{8}$ in. thick, connected to a stalk containing a central duct On section the tumour and duct were found to be lined with mucosa forming villi covered with columnar epithelium and goblet cells, as seen in the small intestine Gastric or colonic mucosa was not seen At the side of the duct was a fibrous cord, probably the obliterated vitelline artery

SUMMARY

A case of patent vitello intestinal duct complicated by prolapse of the intestinal mucosa through the umbilicus, is described.

The child s uneventful recovery after operation suggests that it is best to leave such cases for six months or more before operating Early interference is probably responsible for the high mortality rate in recorded cases (87%)

The obliterated vitelline artery is a potential cause of strangulation, which may necessitate earlier operation

Our thanks are due to Dr G Behr for his pathological report and the photographs, and to Dr J Grieve for the radiological reports.

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TRAUMATIC RUPTURE OF THE BILE-DUCTS

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RUPTURE of some part of the biliary tract is a rare *complication of trauma to the right upper quadrant of* the abdomen Injury to the ducts is less common than to the gall bladder : Rudberg (1921) described a case of injury to the common duct and collected 40 other examples of bile duct injury Lewis (1938) recounting a further case, could only find 6 additional ones since Rudberg s paper Since then 2 more have been reported complete rupture of the common duct (Lysaght 1939) and injury to the common duct associated with tran section of the pyloric part of the stomach (Grimault 1947) Of 54 cases of benign extrahepatic biliary obstruc tion recently described by O Malley et al. (1951) 46 followed some operation on the biliary tract, but not one was the result of non-surgical trauma

CASE REPORT

A farmer s son, aged 22 months, was admitted to Crewe and District Hospital on Feb 24 1952 having that morning been knocked down by a farm tractor a wheel of which passed over his body He had been unconscious for a short time but this phase had quickly passed and he was less shocked than would have been expected. His face, neck, and upper chest were covered with the minute petechiæ of traumatic asphyxia, and there were conjunctival ecchymoses. These signs and slight bruising over the back of the shoulders pointed to a crushing injury of the chest and neither symptoms nor signs suggested an intra abdominal injury. Radiological examination of the chest, pelvis, and skull was negative, and the child at no time showed evidence of any pulmonary affection His condition gradually improved, and by the ninth day the petechiæ had faded Slight conjunctival icterus was then noted On March 5, having been up for a day or two, he was allowed home

That night he came crying into his parents' bedroom It seems likely that he leaned against the side of his cot and fell out on to the floor From that moment his condition changed for the worse, and on March 8 he was brought back to hospital ill, lethargic, and with a distended abdomen Three days later he was jaundiced, his stools were pale, and there was evidence of free fluid in the abdomen Six ounces of turbid bile coloured fluid was obtained by paracentesis, this contained red blood cells as well as bile pigments The boy's condition was complicated by an attack of chickenpox During the latter part of March paracentesis was done three times, 42 oz being obtained on the last occasion Intraperitoneal rupture of a bile duct was diagnosed, the long interval before the occurrence of effusion suggested this rather than rupture of the gall-bladder

Operation (April 4) —A subcostal incision allowed the escape of bile from the peritoneum Separation of omental adhesions below the liver exposed a cavity whose walls were stained intensely green, as, to a lesser degree, were all the abdominal contents Within this cavity bile was issuing from a minute orifice at the porta hepatis A fine probe passed only 8 mm up this sinus, and its exact relationship to the ducts could not be determined, but it was near the junction of the right and left hepatic ducts The gall-bladder, cystic duct, and structures in front of the foramen of Winslow appeared normal Dissection amidst the bile soaked tissues around the orifice was impracticable A short length of 'Polythene' tubing was stitched to the margin and implanted into a loop of jejunum, which was fixed to tissues round the porta hepatis. A side-to side anastomosis between the limbs of the loop was made, and the abdomen was closed with drainage

Recovery —The child stood the operation well, and two days later he passed a normally coloured stool There was little drainage from the abdomen, which, however, remained for some days rather distended Subsequent improvement was rapid A month later cholecystography showed the tube in place but no filling by the dye Recent cholecystography shows similar appearances. In April, 1953, the boy was well and free from symptoms

ÆTIOLOGY

Injury to the bile ducts from external violence is always the result of a blow or crush in the region of the right costal margin Usually this is the only injury, but sometimes there is associated visceral damage Probably the direction of the force rather than its violence determines whether the ducts are injured, Lewis (1938) suggests that the force must be applied in a direction that will crush the ducts between the liver and vertebral bodies

In most case histories in which injury to the bile ducts has been the sole lesion there has been shock of short duration, accompanied by pain in the region of the liver The severity of these initial symptoms varies After an interval, which may be only a day but is usually longer and may be up to a fortnight or even more, jaundice, clay-coloured stools, and bile in the urine are observed, and the abdomen becomes distended This syndrome of jaundice with clay-coloured stools and rapidly increasing fluid in the peritoneum, which aspiration shows to be bile, is pathognomonic of injury to some part of the biliary tract Exhaustion, fever, and loss of weight become apparent, and the patient may soon become critically ill. The extravasated bile may be shut off by adhesions, and a limited swelling in the region of the liver, sometimes described as cyst-like, may be detected Sometimes the accumulation is limited to the lesser sac

In the present case the original extravasation was presumably shut off and became localised to a small cavity in the greater sac below the liver Subsequently, when the child fell from his cot eleven days after the accident, this ruptured, and escaping bile began to fill the general peritoneal cavity A case described by Edington (1933) provides an interesting parallel. Pain and jaundice followed a blow in the hepatic region, but diminished during the third week, and the patient returned to work On the twenty-fifth day, while boarding a tram, he strained himself, his symptoms recurred and subsequent operation revealed an extension of a previously localised extravasation to a much wider area There is an analogy here to the sequence of events in the delayed type of rupture of the spleen

It would be expected that some cases would develop a stricture, and this sometimes happens, though less frequently than after surgical damage to the ducts Perhaps the rent is usually small and involves only a portion of the lumen A stricture of a hepatic duct provides a most difficult problem, and the possibility of this sequel should be an important consideration in deciding the appropriate operation in the early stage Later it may be impossible to expose a strictured duct because of adhesions

PROGNOSIS AND TREATMENT

The *older records show* a high case mortality Aspiration, often repeated many times, was the usual procedure Every case described in the last thirty years has been treated surgically, in most cases bile has been evacuated and external drainage provided I have found no record in which direct repair of a torn duct has been satisfactorily accomplished without subsequent stricture Garré (1908) reported a case in which suture of a hepatic duct apparently succeeded, but a further operation was required a year later for cicatricial contracture at the site of anastomosis In Lysaght's (1939) case complete rupture of the common bile duct was associated with a rent in the duodenum, and retraction rendered repair impossible, he considered that ligation of the duct and cholecystogastrostomy would be simpler than implantation of the upper end into the stomach, duodenum, or jejunum, and this he successfully accomplished Several cases have required more than one operation, one, comparable to mine, of a boy crushed by the wheel of a car, described by Waugh (191 required three operations for drainage, in Edington's case, previously mentioned, thirty-three days after the first operation the biliary fistula was implanted into the stomach, and in other cases the development of a stricture has necessitated intervention after long intervals

It should be an important object of treatment to establish a flow of bile into the intestinal tract as soon as possible Exhaustion and wasting are the inevitable result of continuing loss of all or most of the bile from the body Patients with external biliary fistula improve when the bile is collected and returned to digestive through a Ryle's tube Every effort should be made to ensure that one operation will suffice, subsequent intervention is likely to be difficult and, as in Lewis's (1938) case, adhesions may render it quite impossible to identify important structures In rupture of the common duct ligation of the divided ends and anastomosis of the gall-bladder to the jejunum will usually be the most satisfactory operation Injury to the hepatic ducts presents a more difficult problem Damage is said to occur most frequently near the junction of the right and left hepatic ducts, but it has usually proved impossible to identify the individual ducts or the exact anatomical site of the rupture All that is seen is a little opening from which bile trickles An attempt should be made to provide a channel by which bile can flow into the intestine anastomosis of the fistula to a loop of jejunum succeeded in the present case and appears to be a suitable method o adopt in similar circumstances If this is impossible xternal drainage must be provided with the intention t a later date of implanting the fistula into the limentary tract.

SUMMARY

A case is described of traumatic rupture of the hepatic ucts in a child, treated by choledochojejunostomy

The ætiology clinical findings and surgical treatment re discussed

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THE CLEVEDON POSITIVE-PRESSURE RESPIRATOR

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WHEN Lassen (1953) demonstrated in Copenhagen last ear that positive-pressure respiration combined with racheotomy could save life in certain types of polio nyelitis, it was obvious that treatment of this sort hould be available in this country

Lasson's original method required manual operation of the espirator and an almost indefinite upply of trained personnel The dvantages of an automatic type positive pressure apparatus was vident in Denmark, and Bang 1953) published details of such machine. It is understood that utomatic respirators have now een used in Denmark with arying success In this country Pask (1953) Beaver (1953) and Russell and Schuster (1953) have developed similar equipment. In April of this year we acquired or this hospital a manual respirator such as was used in Denmark, and later added the Oxford inflator described by Macintosh (1953)

Since it seemed very difficult o provide sufficient personnel to perate manual respirators in any umber we constructed an automatic respirator similar to that lescribed by Bang Although Bang described the principles of the apparatus, the engineering details were not defined. With the financial approval of the South Western Regional Hospital Board and the expert assistance of Mr M. J Willcocks of Willcocks (Clevedon) Ltd., Instruments Section, a prototype was produced. Improved patterns were available by the middle of July 1953 We now offer a preliminary report

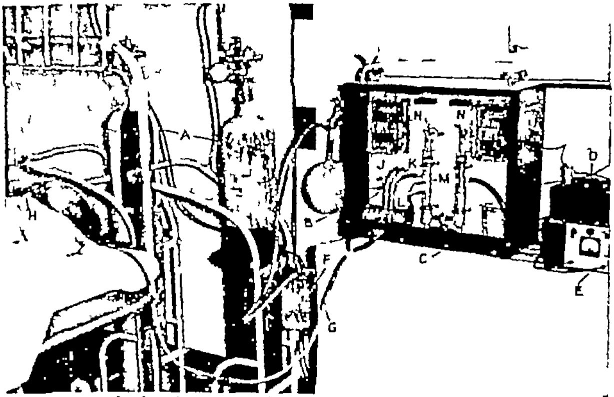
APPARATUS

The characteristics of the apparatus are evident in the accompanying figure It consists of a slide-valve operated by electromagnets which in turn are actuated by electrolytic switches in a U tube partly filled with acidified sodium-sulphate solution The machine is powered by a 12V battery delivering 1 amp maintained by a trickle charger The Clevedon machine is similar to that designed by Bang but the valve gear is original and electrolyte is used instead of floats in the U tube.

Medical air (British Oxygen Co) enriched with oxygen is supplied from large cylinders through a humidifier to a reservoir bag (an ordinary football bladder) and so through the inlet valve of the machine to the patient in a circuit closed by the tracheal tube cuff The pulmonary pressure built up by the inspired air pushes the electrolyte fluid up to the second switch, which opens the expiratory valve thus releasing expired air to the atmosphere The electrolyte falls under gravity to reach the original switch and so opens the inspiratory valve for another cycle The amount of air-oxygen mixture the speed the depth and the inspiration/expiration ratio of respiration can all be controlled The machine is of self-demand type and has an automatic safety valve There is only one moving part, and the valve mechanism can be changed in less than 30 seconds without undoing any nuts or bolts. Relays are used to reduce the current passed by the electrolyte to about 30 mA thus minimising electrolysis and sparking The apparatus is relatively cheap (about £60) is portable, and can operate independently of a main electricity supply

THE MACHINE IN USE

A well-developed man, aged 21 was admitted at 6.30 A.M on Sept 28 1953 with severe poliomyelitis. At 7.30 A.M. he was placed in a Drinker type tank respirator because of partial failure of his respiratory



The apparatus: A, air and oxygen cylinders; B reservoir bag; C, automatic respirator; D battery; E trickle charger; F humidifier; G gas tube to patient; H tracheotomy tube; J gas inlet; K, gas exhaust; L, valve gear; M electrolytic switches in U-tube; N electrical relays.

muscles During the day his paralysis spread, and by 6 P M the respiratory-muscle paralysis was almost complete In addition he had developed bulbar involvement, with inability to swallow, and was accumulating pharyngeal mucus Continued treatment in the tank respirator was obviously going to prove rapidly fatal, since it was impossible to keep the airway clear It was decided to try the positive pressure machine

The patient was transferred to a bed, and respiration was maintained with the manually operated Oxford inflator through a face mask Tracheotomy under local anæsthesia was performed by one of us (J M), a small window being cut in the trachea and a cuffed endotracheal tube inserted This was connected to the automatic respirator and satisfactory breathing was established at once Maximum comfort was obtained with a mixture of 4 litres of air and 2 litres of oxygen a minute at a respiratory rate of 12 breaths a minute The inspiration pressure was 16–20 cm H_2O. With this régime good air entry could be heard throughout all areas of both lung fields The success of the respirator was best shown by the fact that the patient fell asleep for the first time in two days

Nursing was carried out at a postural tilt of about 20°, head down From the beginning there was completely adequate aeration of the lungs

This automatic respirator has maintained the patient's life up to the time of writing, and minor adjustments only have been required For long periods the respirator has worked without attention The patient has been comfortable and cheerful and has had adequate sleep Heavy sedation has not been required Œsophageal tube-feeding was instituted on the second day General nursing, postural treatment, and catheterisation were all easily achieved and found to be a welcome change from the performance of similar tasks in the tank respirator The patient started to recover his ability to swallow on the sixth day, and œsophageal tube-feeding is no longer necessary On the twelfth day some spontaneous respiration recommenced, and now (Oct 27) the patient is able to breathe himself for periods of an hour

Secretions accumulate in the tube and suction of the tube has been necessary at intervals of two to six hours It has only occasionally been necessary to suck out the main bronchi The indications for suction seem to be simply the sound of râles in the tube audible at the bedside or conducted to the lung fields and heard through a stethoscope There have been no signs of fluid accumulating in the smaller bronchi or alveoli The endotracheal tube has been changed about daily

Although the difficulties of management have been considerably less than anticipated, there has been a doctor present in the ward at all times, and we feel that this is essential for safe supervision

SUMMARY

A positive pressure respirator which has only one moving part and works independently of a main electricity supply is presented

A case in which it is still being used is described

Our sincere thanks are due to Mr M J Willcocks and his many colleagues for the generous help and beautiful engineering technique which they have put at our disposal in producing this machine

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Medical Societies

BRITISH ORTHOPÆDIC ASSOCIATION

THE association's annual meeting was held at Birmingham on Oct 23 and 24 SIR REGINALD WATSON-JONES was in the chair on the first day, and on the second day he was succeeded by the new president, Prof BRYAN MCFARLAND

For the first time in the association's history an instructional course in orthopædic surgery was given on the day before the meeting This course was attended by nearly two hundred young surgeons and senior orthopædic registrars, as well as by some of the fellows and members of the association

Presidential Address

SIR REGINALD WATSON-JONES, the retiring president said that the association had created strong ties between the orthopædic surgeons of Great Britain, the Commonwealth countries, and the U S A, it had given strong support to the foundation of the New Zealand Orthopædic Association and the South African Orthopædic Association, and with equal generosity from the United States and Canada had secured the foundation of travelling fellowships for young orthopædic surgeons between the United States, Canada, and Britain, with a share by other countries of the Commonwealth

The association, mindful of the value of tradition, had recently taken steps to stimulate interest in historical treasures relating to orthopædic and allied subjects. A collection of such treasures was to be housed at the Royal College of Surgeons of England, where a selection would always be on view in the college hall

Acrylic Replacement in Fractures of Femur

Mr DAVID LE VAY described his experiences with replacement arthroplasty of the hip by a prosthesis of the Judet type as the primary treatment of subcapital fractures of the neck of the femur The method was well justified in the elderly Most patients had been allowed up 4–5 weeks after the operation, and the average length of stay in hospital was 10 weeks Although there had been a tendency for the head to migrate into a varus position a point of stability was reached beyond which no further displacement occurred Insertion of the prosthesis to lie in slight valgus offered advantages

Mr O J VAUGHAN JACKSON, who had done replacement arthroplasty in 34 cases, suggested that it was still too early finally to assess its merits At best it did not give a normal joint, which was not true of a successful nailing operation it could therefore not be recommended for all patients with femoral neck fractures—certainly not for those in their fifties or sixties Of his 34 cases, the operation was tolerated well in 32 and poorly in 1, 1 patient died The main local complication was fracture of the prosthesis (4 cases), the use of metal prostheses in place of plastic would probably solve the problem of breakage Walking was resumed 5–6 weeks after operation Most patients preferred to use sticks for at least 6 months but none complained of severe pain

Mr G N GOLDEN (Guildford) reported 60 cases of Judet arthroplasty for fracture which he had reviewed in collaboration with Mr C C M Murray (Southsea) and Mr A. G Ord (Portsmouth) The results were good in 70% and satisfactory in a further 15%

The Valgus Foot

Mr G K ROSE (Shrewsbury) said that the dividing line between the normal and the "valgus" or "pronated" foot was ill defined, and the indications for treatment indefinite. He had undertaken a long term investigation of the feet of 1 children aged 6–8 years His conclusions were that some valgus shift was normal, but that there was no difference in the valgus index between boys and girls The significance of valgus shift was greatest when the axis of the knee was medial to that of the foot and least when the axis of the knee was lateral to that of the foot The essential pathological feature in the abnormal valgus foot was strain of the peritalar joint, not simply an abnormal position of the joint

Causes of Coccydynia

Mr H. J Richards (Oswestry) reviewed the possible causes f coccydynia in the light of a study of 102 cases. A history f injury was present in less than half the cases. Infection nd neoplasm were occasional causes; psychogenic factors ere secondary rather than primary He believed that in any cases coccydynia was caused by a central prolapse of ne of the lower lumbar intervertebral discs. Of 1000 patients iagnosed as having a disc protrusion, 40 complained of occydynia associated with sciatic pain; of the patients with occydynia nearly half had initial low backache or sciatica, nd most of the remainder later developed similar symptoms.

Mr K. I. Nissen expressed strong disagreement with Mr Richards's hypothesis. In his experience relief from coccy ynia could nearly always be assured by repeated manipulation f the coccyx: excision might be necessary in 5–10% of cases

Fractures of Lateral Condyle of Humerus

Mr J N Wilson (Cardiff) reviewed 57 fractures of the ateral condyle of the humerus in children. He recognised hree types (1) the flake fracture in which a thin piece of one was detached from the bony nucleus of the capitulum; 2) the type in which a large fragment was avulsed; and 3) the fracture with subluxation of the elbow joint. The ollowing complications were observed limitation of move ent (uncommon); deformity; ulnar neuritis; non union 1 case); and loose body In treatment, conservative methods ere usually successful

Professor McFarland advocated a cautious attitude owards the immobilisation of injured elbows in plaster

Treatment of Peripheral Arterial Disease

Prof. F A. R. Stammers (Birmingham) said that the vascular conditions that might be benefited by sympathectomy could be classified under five headings: (1) those from spasm (impaired circulation after poliomyelitis, acrocyanosis frigida, Raynaud's disease); (2) those from such anatomical abnormalities as cervical rib; (3) those from disease of the arterial wall with superimposed spasm of various degree (Buerger's disease, endarteritis, medial sclerosis atherosclerosis); (4) conditions caused by embolism; and (5) conditions caused by injury In the treatment of peripheral circulatory impairment the first aim was to remove spasm and promote collateral circulation Smoking should be absolutely prohibited (not just reduced) but alcohol was beneficial. Reflex vasodilatation by general body heating was a useful method of treatment Buerger's exercises and antispasmodics were worth a trial Operation should be considered when conservative measures were ineffective In general lumbar sympathectomy was more successful and more permanently effective than cervical sympathectomy In the treatment of intermittent claudication severance of the tendo calcaneus was of use only in the elderly it converted a painful hobble to a painless shuffle.

Muscle "Spasm" in Poliomyelitis

Mr G P Mitchell (Oxford) said that in his experience of the early stages of poliomyelitis there was no true spasm except in the spinal muscles during the stage of meningeal irritation. In the limbs, limitation of passive movement was the consequence not of true spasm but of the resistance of muscles to stretch The movements that were most restricted were those that caused traction on the main limb nerves, and if the liability to traction was increased by changes of posture—such as lateral flexion of the neck to the opposite side in cases of restricted elbow extension—the resistance to stretch was increased. Muscle resistance to stretch was simply a guarding reaction to prevent traction on the limb nerves.

Prof J Trueta (Oxford) considered that these observations solved the hitherto baffling problems of so-called muscle spasm in poliomyelitis.

Congenital Dislocation of Hip

Mr E W Somerville (Oxford) believed that in congenital dislocation of the hip the main factor responsible for the initial subluxation (which later progressed to complete dislocation) was anteversion of the femoral neck in consequence of which the femoral head exerted pressure on the anterior part of the capsule when the limbs were extended after birth. (Pressure was minimal while the limbs remained flexed so that dislocation before birth was unlikely) If the capsule stretched under this pressure the femoral head was extruded from the front of the joint and lay at first antero superiorly on the ilium. There it was so placed that the trochanteric region, by pressing upon the fibrocartilaginous limbus of the acetabulum, turned it over into the joint where it occupied the supero posterior part of the cavity and formed the chief obstacle to complete reduction of the dislocation by manipulation In every patient operated on he had found the limbus inverted as described, and he had produced an identical inversion of the limbus experimentally in a cadaver His plan of treatment—which was still on trial and was not yet advocated for general use—was to remove the inverted limbus, thereby allowing complete reduction of the dislocation and subsequently to do a rotation osteotomy of the femur to correct the anteversion and thereby prevent recurrence of the dislocation. The stage of unrestricted walking was reached within four months of the beginning of treatment So far, the results were promising

Mr H. J Seddon could not readily accept the hypothesis that the limbus played such an important part He preferred to rely on conservative treatment so far as possible; operation should be reserved for cases that were unsuitable for conservative treatment

Mr G C Gordon (Keswick) recalled that joints were formed at the 8th week of intra uterine development. He showed radiographs of a congenitally dislocated hip in a fœtus at the 28th week of gestation.

Isoniazid in Skeletal Tuberculosis

Mr A. G Quinlan (Oswestry) reviewed the results of isoniazid therapy continued for 6 months in 20 cases of skeletal tuberculosis. The drug distinctly improved the patient's general condition, but had no dramatic effect upon the tuberculous lesion.

Dr F Harwood Stevenson (Stanmore) suggested that streptomycin, *p*-aminosalicylic acid (P.A.S.) and isoniazid should always be used together to minimise the development of bacterial resistance

Mr M. B Devas reported that 10 patients with skeletal tuberculosis who had received a combination of streptomycin P.A.S., and isoniazid for 6 months all tolerated the drugs well, and in all cases the lesion was quiescent a year later

Foot Supports

Mr Norman Capener (Exeter) said that the association's subcommittee formed to study surgical appliances and splints was anxious about the promiscuous dispensing of foot supports "over the counter" When these were required for feet that were structurally abnormal, they should be made individually from plaster casts of the feet. When the feet were structurally within normal limits, he doubted the wisdom of prescribing foot supports at all.

Scoliosis

Mr F G Allan (Birmingham) described a new method of correcting scoliotic curves. In principle, the method consisted in the use of an extensible jack operated by a screw mechanism. Each end of the jack was designed to fit into the side of a vertebral body at its junction with the transverse process. The jack was so placed that it bridged the primary curve on its concave side. When in position it was extended by screwing the centre-piece with a tommy bar thereby reducing the curve Later a segment of the spine was fused by bone grafts. The method had the advantages that no plaster fixation was needed before or after operation, and that the time occupied by treatment was much reduced compared with correction by hinged plaster jackets. Moreover it had been possible to correct curves that looked incorrectible by ordinary methods. The operation had proved easiest in cases of lumbar and thoracolumbar curves. It was relatively difficult in thoracic deformity but the only complication of note had been pneumothorax from perforation of the pleura.

Mr H Osmond Clarke welcomed the report as a likely step towards the solution of the problem of scoliosis, especially in younger children in whom the recognised methods of treatment were notoriously unreliable

Primary Dislocation of Patella

Mr J S Ellis (Southampton) believed that primary lateral dislocation of the patella was commoner than was generally realised. It might explain some cases in which full function was restored after excision of a normal cartilage when the symptoms had been attributed erroneously to a torn cartilage Only occasionally did the dislocation persist usually spontaneous reduction occurred, and the diagnosis was then difficult The history might be like that of a case of torn medial cartilage; but there was hæmarthrosis (unusual with torn cartilage) and the tenderness, although on the medial side, was not localised to the level of the joint line A diagnostic sign was the pain produced by attempts to push the patella laterally At operation a rent in the capsule medial to the patella was to be expected When the condition was recognised soon after the injury operative repair, with pleating of the medial part of the capsule, should be considered

Dorsal Adduction Deformities of Fifth Toe

Mr W H Scrase (Birmingham) said that, in the treatment of dorsal adduction deformities of the fifth toe, manipulation and splintage were time consuming and seldom gave more than temporary benefit Amputation was often unacceptable to the patient, and it might predispose to tenderness over the fifth metatarsal head The technique described by Lapidus, which combined capsulotomy with transfer of the long extensor tendon to the plantar aspect of the phalanx, seemed attractive but he had little experience of it The method of skin advancement by V-Y plasty was said to be successful, but he had seen cases in which the deformity had recurred The operation that he had used was "syndactilisation" of the fifth to the fourth toe The extensor tendon was divided and the base of the proximal phalanx of the fifth toe was excised, the adjacent surfaces of the fourth and fifth toes were united after excision of a fillet of skin The results were good in 39 and fair in 3 of the 42 toes operated on

Mr J N Wilson (Cardiff) defended the operation of skin advancement by V-Y-plasty Professor McFarland claimed a long experience of the "syndactilisation" operation, which he had found satisfactory

Paralytic Dislocation of Hip

Mr G Blundell Jones (Exeter) described 12 cases of paralytic dislocation of the hip, in 7 of which this was bilateral The causes were spastic hemiplegia or paraplegia, poliomyelitis, and meningomyelocele In all of these patients the onset had been before the age of 2 years Mr Blundell Jones believed that the factor mainly responsible for the dislocation was an abnormal valgus position of the neck of the femur, which was often almost in line with the shaft Adductor contracture was a contributory cause After dislocation the acetabulum gradually became more shallow, but it retained useful depth for several years In the early stages the dislocation could be reduced by simple traction and abduction of the limb, but it was likely to recur Later, secondary contractures prevented reduction When the dislocation was reducible the hip had been made stable by wedge osteotomy at the base of the neck with restoration of the neck shaft angle to 120° The fragments had usually been fixed after osteotomy by a small nail plate

Mr Le Vay preferred to treat dislocations of this type by a shelf operation, which obviated shortening, preserved the efficiency of the abductor muscles, and did not endanger the blood supply of the femoral head But Mr Blundell Jones did not accept these arguments He had found the wedge osteotomy an easy operation, whereas it was difficult to construct a satisfactory shelf in the correct position He had not found that osteotomy at the base of the neck endangered the blood-supply of the femoral head

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Reviews of Books

The Gold-Headed Cane

7th ed William Macmichael, M.D Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1953 Pp 222 47*s* 6*d*

This is an American reprint of the fifth edition which was published in 1923 The choice of edition is wise, for George Peachey's introduction and biographical notes enrich William Macmichael's text

Macmichael was registrar at the Royal College of Physicians of London when Matthew Baillie's widow presented the cane, a short time before the opening of the present building in 1825 The book takes the form of an autobiography of the cane, which was owned successively by John Radcliffe, Richard Mead, Anthony Askew, William and David Pitcairn, and Matthew Baillie The cane moved in the highest medical circles for a period of 130 years—from a few months after the accession of William and Mary to the middle of the reign of George IV—and it records engagingly the changing pageant of medical practice, besides giving interesting accounts of the foundation and history of the Royal College of Physicians and of the Royal Society

Somewhat oddly, in this reprint the picture of the original cane has been replaced by a plate of a gold-headed cane of different pattern presented to the outstanding medical student of the year at the University of California But we must be grateful to Prof W J Kerr, the new editor, for bringing a delightful book to the notice of a new generation of medical men and students

Pathology in Surgery

Edwin F Hirsch, PH D, M.D, director of the Henry Baird Favill Laboratory and pathologist of St Luke's Hospital, Chicago, Ill Baltimore Williams & Wilkins London Baillière, Tindall, & Cox 1953 Pp 647 76*s* 6*d*

Dr Hirsch's book is essentially pictorial for the text is concise and at times rather too elementary It could be used with advantage by senior students on those occasions when speedy revision of the subject of surgical pathology is unavoidable There are references at the end of each chapter, but they are few and hardly representative The eight coloured pictures are very good and the photomicrographs clear and helpful The reproductions of the gross specimens, however are occasionally disappointing, though great care has been taken in the selection of material

Dr Hirsch has made good use of his own experience, and students will be grateful to him for drawing attention to possible pitfalls which await the unwary—as for instance, that endometriosis is liable to be mistaken for carcinoma of the rectum, and a syphilitic lesion of the cervix uteri for carcinoma.

Lewin's Field Theory in Social Science (London Tavistock Publications 1952 Pp 346 21*s*)—It is still too early to assess the value of Kurt Lewin's contribution to social theory His stimulating personality, his experimental flair, his challenge to the Freudian use of a historical approach to psychological dynamics, and the devotion of his pupils, made him a prominent figure in American psychology Of his writings available in English most have reported work that he and his pupils did while he was still in Germany The present volume, edited by Dorwin Cartwright, shows how productive were his years in the United States, not only in tackling practical problems (such as an earlier collection *Resolving Social Conflicts*, described more fully) but also in developing his theoretical position Papers on the philosophy of science, written between 1940 and 1943, are followed by studies in learning, regression, social experiment, and group dynamics, the general outcome of his researches is presented in the final chapter Lewin's style in writing was dry, giving no hint of the attractiveness of his personal exposition of a problem. But the straightforward account of his views set out in this collection makes it plain that during the last seven years of his life he was an original and fertile influence on the development of social psychology

Diseases of Children (5th ed London Edward Arnold 1953 Pp 1973 £7) —In the six years that have passed since the last edition, much has happened that calls for notice in the revision of this splendid textbook, now edited by Prof Alan Moncrieff and Dr Philip Evans The sections that have been entirely rewritten include those on the causes of congenital malformations, on growth and development, on drug treatment, on kwashiorkor, on endocrine disorders, on diseases of the teeth and jaws, on the alimentary canal, on congenital heart disease, and on infant feeding As before, the book is in two volumes, but the page numbers now run on and there is only one index

Textbook of Medical Treatment (6th ed. Edinburgh and London E & S Livingstone 1953 Pp 1021 60*s*)—Reviewers have spoken so highly in the past of one of the most popular of textbooks that there is really no more to add to the observation that it is living up to its reputation. But we should perhaps note that the complete revision that has lately been made has introduced new chapters on chemotherapy, rehabilitation, the treatment of poisoning, and the chemotherapy of malignant disease, and the book has been reindexed to make the reader's way even smoother The editorial team is unchanged—Prof D M Dunlop, Prof L S P Davidson, and Sir John McNee

THE LANCET

LONDON SATURDAY NOV 7 1953

Winter Admissions to Hospital

EACH winter hospitals up and down the country ickle the recurring problem of finding beds for many xtra patients. Most of these have acute respiratory isease or heart-failure precipitated by bronchitis, nd sometimes their numbers are swollen by an nfluenza epidemic or other episode, such as last ear's catastrophic fog[1] The burden has usually allen mainly on the regional board hospitals—n other words the former local authority and maller voluntary hospitals—which perforce have ad to restrict surgical admissions, whereas in the eaching centres the impact of this additional work vas hardly felt at all. In 1951, however, the Emergency Bed Service introduced for the London rea a new warning system[2] for reducing, in times of tress, the number of non urgent admissions, and n this the teaching hospitals have participated to a arying extent. This system depends on the proortion of patients, referred by practitioners, for hom admission is secured. In the summer the E.B.S normally secures admission for about 90% f cases, the remaining 10% of applications being vithdrawn for one reason or another

> A *white* warning issued when the admission rate falls o 85% is intended as a preliminary alert.
>
> A *yellow* warning goes out with a fall in the admission ate to 80%; and on its receipt various steps may be aken to increase the number of available beds—includng, for example, the prohibition of closure of wards or cleaning a percentage reduction in cold surgery, nd reduction of admissions for investigation
>
> On receipt of a *red* warning, which goes out when the dmission rate falls to 75%, these measures are ntensified

Last winter, in its first real test this system proved its worth but some modifications have been necessary[3] since warnings tended to be issued too late and taken off too soon. There were two reasons for this defect Firstly as pressure on the service mounted, an increasing proportion of cases were admitted by the 'medical referee' procedure—which had the effect of keeping up the admission rate but of delaying the issue of warnings until the situation had become serious Secondly the response of hospitals to the yellow and red warnings caused a sharp rise in the admission rate and thus the warning might have to be cancelled even though applications were still increasing Henceforth for the purpose of warnings, cases admitted through the medical referee will not be included and warnings will not be cancelled until the 'voluntary-admission rate' (i.e excluding those arranged through the medical referee) has risen to 1% above the rate at which it was imposed and applications have fallen to the level at which they stood when the warning was issued Furthermore a white warning will be issued at the request of the Ministry of Health when it has evidence of an imminent emergency, such as an influenza epidemic

Possibly a better index of shortage could be obtained from a group of regional board hospitals than from the E.B.S figures Refusal of E.B.S cases is not necessarily a reliable index of bed occupancy Each regional board hospital receives from its own area many of the less "popular" cases including illness in the elderly and abortions, and if it opens its doors to similar cases from other parts of London it will soon have no room left for its other local commitments Thus refusal of E.B.S cases may not always be related to the immediate bed state.

In the past many hospitals have not appreciated the need for radical rearrangement to deal with winter epidemics Flexibility in the distribution of beds between surgeons and physicians is essential, and yet this distribution has remained remarkably rigid perhaps partly because of considerations of departmental prestige or the seniority of the various members of the medical staff Additional medical beds are an imperative need in the winter, and this seasonal addition could be offset by an excess of surgical beds in the summer months A further difficulty is that of ensuring a proper balance between the claims of semi urgent admissions and those of patients on the waiting list Some restriction of admissions from the waiting list is inevitable but patients whose condition is steadily deteriorating should not have their admission deferred for weeks on end as happened in some hospitals last winter To stop all admissions from the waiting list is not justifiable except for very brief periods It is invaluable to have a fairly senior member of the medical staff charged with the task of striking a balance between elective and emergency admissions Extra beds are no solution. In a winter epidemic, casualties among the nurses are often numerous, and overloading a hard pressed staff simply slows the turnover The most promising course is not to increase the number of beds, but to increase turnover by discharging patients more promptly This involves either securing closer liaison with general practitioners, as has been done at Cambridge,[4] or else making fuller use of convalescent homes. It is unfortunate that at present a convalescent home cannot be related to a particular hospital, for this would greatly aid the early transfer of patients In London much closer coördination is needed, too between outlying hospitals and those in the central area, last winter beds in peripheral hospitals were sometimes empty at a time when central hospitals had more to do than they could manage. The task of admissions officers would be made much less difficult by partial restoration of the arrangement whereby local authority hospitals were responsible for emergencies from a given district It would be wrong however to insist that all emergencies should be geographically distributed and indeed a greater number of acute cases could with advantage be admitted to the central London teaching hospitals (The regional medical admissions officer attached to the E B S represents only the four Metropolitan regional boards and has no authority to secure admissions to the teaching hospitals) It is particularly important that responsibility should be firmly imposed and accepted for the less "popular" group of cases

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[1] See Abercrombie G F *Lancet* 1953 i 231
[2] See *Ibid*, 1951, ii 439
[3] *Ibid* Oct. 31 1953 p 934
[4] *Ibid*, 1951 i, 783

Now is the moment for every medical staff committee to review its arrangements in the light of last winter's experience, and to see that the hospital's resources are equated as closely as possible with the fluctuating needs of the population it serves

The Lethal Aerosol

WHILE public bodies debate the type of masks to be worn, and fashion designers plan fancy little yashmaks, the urgent question arises Can any sort of face covering, likely to be worn by the public, provide significant protection against the hazards of fog inhalation ? To answer this we need to know what the toxic agent is, how it is carried, and where it lodges in the respiratory tract There are several sources of information to which we can turn[1-8] Elaborate studies have been made in Los Angeles of the smoke-fog (the original "smog") so prevalent there[2], but this is rather different from our own polluted fogs, since it consists of smaller particles often in relatively dry air (25–30% relative humidity), the most noticeable effect of which is eye irritation Secondly, there is the Meuse disaster of 1930, when intense cold joined with fog and heavy pollution to produce a suffocative bronchitis, which killed 64 people[3] Investigators attributed the disaster to sulphur dioxide and its oxidation products in the air, and remarked that inflammatory changes in the lungs were slight and that adrenaline injections gave some relief Thirdly, at Donora, Pennsylvania, in 1948, there was again cold, fog, and serious pollution, leading to the death of many asthmatic or cardiac patients[4] Here it has been suggested that the deaths, which could not be ascribed to any single pollutant, were due to synergism between all the various contaminants It was noted, too, that the death-rate fell before the pollution began to lessen Fourthly comes London's experience last winter, when cold, fog, and an increase of sulphur dioxide and smoke in the air coincided, producing an enormous rise in mortality, particularly of elderly chronic bronchitics[5,6] RUSSELL's[7] careful statistical analyses of earlier London fogs had established a correlation between cold and fogginess on the one hand, and respiratory mortality on the other, and cold appeared to be the more important of the two factors All these accounts explain the general conditions that are likely to kill our bronchitics in winter-time, but they hardly supply the information necessary for effective preventive measures Until our fog has been properly analysed for particle distribution and constitution, we must proceed by intelligent guesswork

Fog consists mainly of watery droplets, 5–50 μ in diameter[1] Probably in such saturated air most of the enormous range of different kinds of nuclei (dusts, smokes, pollens, &c) normally carried in the air will have become centres of condensation, thus we shall be dealing principally with a gaseous phase in which watery droplets are suspended Secondly, if there is any water-soluble gaseous contaminant, such as sulphur dioxide, this will tend to dissolve in the droplets, so that the droplets will contain within them the bulk of the water-soluble material in the air This may be of fundamental importance Sulphur dioxide dispersed as one part per million throughout a gaseous phase might be relatively safe, but dissolved in droplets giving a local concentration thousands of times greater, it will produce a strongly acid respiratory rain, which may readily produce bronchial spasm and œdema Already, in fact, there are indications that, for the same total sulphur-dioxide content, a sulphur dioxide aerosol is more dangerous than the gas[9], and no doubt this would also be true of other pollutants Thirdly, droplets of this size will largely be retained in the respiratory tract—the largest in the nose, the smaller ones reaching the bronchioles Particles much smaller than this will tend to escape[10] We may therefore take it, as a working hypothesis, that the danger of these polluted fogs is due to inhalation in unusually cold inspired air of small droplets containing water-soluble pollutants in concentrated form, of such a size as to be retained in the respiratory tract and able to penetrate at least as far as the bronchi and bronchioles

Fortunately fog droplets are relatively large compared to bacteria and smokes A gauze mask or a woollen scarf could be expected to exclude a reasonable proportion—perhaps a half to three quarters—of the particles, which might be enough to bring the pollution of inhaled air below the margin of danger Complete purification is obviously too much to hope for The more layers of gauze used, the more efficient the mask will be, but a balance will have to be struck between efficiency and resistance to breathing The scarf or mask will serve a second purpose, warming and humidifying the incoming air Indeed, as the mask becomes sodden with expired condensation it may also come to serve as a watery "scrubber" of the gaseous phase, although at the same time its resistance will rise A gauze mask or, possibly better, a thick woollen scarf wrapped round the face, by excluding droplets and by warming and scrubbing the inhaled air, may, so far as can be judged, really prove useful The only obvious danger seems to be too great a respiratory resistance in a patient already breathing with difficulty Possibly, considering RUSSELL's analysis, warming the air is as important as filtering it A bronchitic's room should obviously be well heated, even if he cannot wear a mask, and, as CROWDEN points out,[11] the method of heating should not entail sucking in more fog from outside, electric radiators are particularly suitable

This discussion of therapeutic (as against preventive) measures can only be tentative, so long as the exact constitution of the fog and its lethal principle remains unknown There exists a rich store of experience from industrial and military research in making smokes and aerosols and in devising protection against them This experience should now be mobilised against an enemy long unchallenged

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Dextran

Reports on the clinical use of dextran have shown hat the risk of reactions after its infusion is slight Iost of the reported reactions have been febrile, rticarial or allergic reactions have been few When, owever, dextran is injected into healthy people, he story is rather different As was first observed n America, nearly 50% of healthy recipients may how reactions of one kind or another and the incidence seems to be related to the type of dextran used On an earlier page Mr Wilkinson and Dr. Storey escribe the results of infusing 500–1000 ml of a olution of closely fractionated dextran into 5 normal olunteers with normal blood volumes All 5 showed eactions, which can be roughly divided into two hases The first which developed during or soon fter the infusion and lasted up to two hours, was redominantly urticarial, the second usually eveloped later and was characterised by vasomotor nstability Wilkinson finds that the later phase oincides with a decrease of the plasma volume below he pre-infusion level. This was observed in all the ubjects within about two and a half hours of ompleting the infusion and was accompanied by the movement out of the vessels of up to 30% of the total irculating albumin and dextran Thereafter dextran e-entered the circulation, and the total circulatory protein was greater than before the injection, the plasma volume increased and remained above the pre-infusion level for many hours During this last eriod the volunteers complained of fullness of the ead, precordial pain, and breathlessness on exertion Wilkinson has given the same solution of dextran o "shocked" patients (he does not say how many) with only 2 mild and transient reactions

Heistø and Lund [1] have described a somewhat similar sequence in 20 normal people, each of whom was given an infusion of 1000 ml. of one of eight different batches of dextran, derived from different strains of *Leuconostoc mesenteroides* and prepared by acid hydrolysis or thermal or ultrasonic degradation. Reactions broadly similar to those now described by Wilkinson were noted in 15 of the 20 subjects In 13 the reaction was accompanied by diminution of plasma volume (after an initial increase) below the original level and decrease of total circulatory protein. In non reactors and 2 of the reactors the plasma volume was increased during the five hour period of observation and there was no appreciable change in total circulatory protein Heistø and Lund found that the incidence of reactions was related to the strain of *L mesenteroides* used in preparing the dextran, but not apparently to the method of preparation Neill and Abrahams [2] have demonstrated cross-reactions between antisera to *Salmonella typhi* and other members of the salmonella group, and native and clinical dextrans and Heistø and Lund say that in their study the severity of reactions seemed to be related to the time which had elapsed since T.A.B inoculation. This however may have been fortuitous for the number given each type of dextran was small. In a larger American series [3] no relation could be found between the number and type of prophylactic inoculations and the incidence of reactions Like Wilkinson, Heistø and Lund found that their batches of dextran could be given without ill effect to patients with oligæmic shock.

Kabat and Berg [4] and Maurer [5] have investigated a large number of native and clinical dextrans and have shown that these, given in 1 mg doses subcutaneously to normal individuals, are antigenic, judging by the development of precipitins and cutaneous sensitivity of the weal and erythema type Precipitins and positive skin reactions were found in some of the volunteers before the dextran was injected, indicating that they had already been immunised by some means These workers conclude that the dextrans themselves were antigenic and that the antigenicity was not attributable to linkage to protein or some prosthetic group This antigenicity seemed to be related to the chemical structure of the dextrans, some of which evoked less antibody than others The numbers of subjects injected with each dextran were too small for conclusions on the relative antigenicity of each batch or on the proportion of normal people who are already sensitised. If, as Maurer suggests some people do not respond to dextran as an antigen the interpretation of the results is all the more difficult since the proportion of non reactors is unknown Kabat and Berg suggest that the urticarial or allergic reactions observed after injecting dextran in normal people, or in patients are probably caused by the presence of antibodies to dextran Maurer considers that antibodies to pneumococcal polysaccharides, types II, XII, or XX, which are known to give cross reactions with dextran, are probably not of great clinical significance, since he found that the anti dextran antibody nitrogen levels were much the same before and after absorption with these polysaccharides Neill et al [6] have shown that dextran is a common contaminant of commercial sugar, and Hehre and Neill [7] have isolated dextran producing organisms from the human intestine Kabat and Berg, and Maurer, suggest that in certain circumstances either or both of these factors may possibly provide an antigenic stimulus so that antibodies to dextran are formed

It seems clear that some people are sensitive to certain kinds of dextran, but the response to a small dose of antigen is not necessarily the same as that elicited by a large dose. Felton and Ottingen [8] have described a state of "immunological paralysis" with polysaccharide antigens In patients the response to an antigen may be altered by the disease or by anæsthesia. Dextran solutions of many kinds have been given to thousands of patients and it is most important to know whether any have become immunised So far as we know, there have been no reports on the effects of second infusions of dextran in patients, or of observations designed to show whether any patients given an infusion of dextran become sensitised and show the type of response described by Kabat and Berg and by Maurer. The lack of adverse reports may indicate that very few patients, or none, are sensitised by an infusion

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of dextran This is supported by a series of observations on normal individuals in America [9] which showed that second infusions of dextran four to twenty-three months after the initial infusion were not followed by systemic reactions, except in those who had reacted to the first infusion, and in these the reactions to the second infusion were not more severe than the reactions to the first Furthermore, the incidence of positive reactions to the intracutaneous injection of dextran in people who had previously been given an infusion of dextran was the same as in persons who had never been given dextran This indicates that infusion of dextran had not given rise to true sensitivity

There is still much to be learnt about dextran Certain strains of *L mesenteroides* are poor antibody producers in animals, it would be worth investigating whether the corresponding dextrans are only weakly antigenic or even non-antigenic in man There is evidence that the antigenic response is influenced by the chemical structure of the dextran and possibly also by its molecular size, and varying the composition of the medium in which the organism is grown is known to affect the chemical structure of the dextran produced Further study of this aspect would seem worth while Furthermore, it would be valuable to secure agreed physical and chemical methods for characterising the many different dextrans, many reports give insufficient information for the dextran to be identified

In the last five years dextran has been investigated more intensively than probably any other plasma substitute, and the story, in unfolding, has gradually become more complex As examination of the other plasma substitutes progresses, a similarly involved picture is likely to develop Some of the new information about dextran merits careful thought, but the clinical evidence suggests that dextran solutions can be administered safely

Facts from General Practice

Two factors are helping to secure for general practice the prominence it has always deserved but which it was in danger of losing One is concern over the increasing cost of the hospital service and the tardy realisation that, if the general practitioner is to check this drain on national resources by himself investigating and treating illness in its early stages, he must receive both credit and help—including access to investigation departments The other factor is a new awareness that, in our preoccupation with hospital techniques, we have been neglecting first causes in the home and the place of work Had research into these causes been pursued as vigorously as that into the causes of infectious diseases, the total of our people's ills might now be less, and if this backwardness is to be ended we shall have to look largely to the general practitioner, who is better placed than most to study the influence of heredity and environment on health and disease in the individual and the family Here again he needs help, and he needs, too, the opportunity to coöperate with his fellows Fortunately, both are likely to be obtainable through the College of General Practitioners [10]

But if the family doctor is to make a serious incursion into this field, he must know the extent of morbidity in the population, and the contribution of each disease to the total—a subject on which we still have little precise information As a source of the essential knowledge the experience of general practitioners themselves is necessarily imperfect, but it is about the best we have at the moment A first attempt to tap this source is recorded in a report,[11] issued this week, in which Dr W P D LOGAN, chief medical statistician of the General Register Office, sets out the results of a year's experience (from April 1951) in eight widely different practices The eight practitioners recorded the date and place of consultations, certificates issued, referral to hospital or elsewhere, and diagnosis or other reason for consultation These data have yielded information which, though it may not apply to the country as a whole, goes some way to replace impressions by facts

Reasons for consultation.—The two diseases responsible for the largest proportions of consultations were acute nasopharyngitis (common cold) (60 9 consultations per 1000) and bronchitis (53 0 per 1000), additional to the latter were acute bronchitis (4 9) and chronic bronchitis (10 8), giving a total for bronchitis of all kinds of about 68 7 per 1000 Next came influenza (26 5) and acute tonsillitis (22 1) Other conditions that accounted for more than 10 consultations per 1000 total were asthma (10 5), asthenic reaction (neurasthenia, &c) (11 1), otitis media (19 7), hypertension (16 3), pneumonia (12 4), gastritis (11 9), functional gastric disorders (indigestion, &c) (14 1), gastro-enteritis (12 6), boil and carbuncle (15 6), dermatitis (10 2), muscular rheumatism (16 0), "rheumatism" (15 0), cough (11 4), and routine antenatal examinations (19 4)

Respiratory diseases accounted for 24 % of all consultations, digestive diseases for 9 %, diseases of the nervous system and sense organs for 8 %, circulatory, locomotor, and skin diseases for 7 % each, infectious diseases for 6 %, and injuries for 5 % Allergic and endocrine diseases and genito-urinary disease were each responsible for 4 %, the mental and psychoneurotic group for 3 %, and neoplasms, blood diseases, and maternal complications each for 1 % Symptoms and senility accounted for 8 %, and reasons other than sickness for 5 % of the total

Sex differences —Three out of every five consultations recorded were in respect of female patients, but, taking account of their larger numbers in the practice populations, this excess was only 25 %

Place of consultation —68 % of all consultations were surgery attendances, 27 % were home visits, and 5 % took place elsewhere

Certificates —The diseases that accounted for the largest proportions of certificates (including National Health Insurance, private, and other certificates) were:

	Proportion per 1000 total certificates	
	Male	*Female*
Psychoneurotic disorders	17 7	43 8
Acute nasopharyngitis	46 3	70·0
Acute tonsillitis	20 7	28·0
Influenza	80 9	54 1
Bronchitis	91 3	53 1
Ulcer of stomach and duodenum	40 6	11·6
Fibrositis	27 4	18 2
Maternity antenatal	—	35·4

Of all certificates issued 29 % were for respiratory disease—well over twice as many as for diseases of the digestive system, which were the next most common reason for issuing a certificate Certificates for non medical pur-

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9 Report to National Research Council Washington April, 1952

10 College of General Practitioners First Annual Report, 1953 Oct 31, 1953 p 924

11 General Register Office Studies on Medical and Population Subjects no 7 General Practitioners' Records An analysis of the clinical records of eight practices during the period April 1951 to March, 1952 By W P D LOGAN, M D, PH D chief medical statistician General Register Office, with a foreword by Sir John Charles M D F R.C.P chief medical officer of the Ministry of Health H M Stationery Office Pp 131 8s 6d

oses (e.g , countersigning of claims for family allow nces old age pensions and tobacco tokens) accounted or only 0 3% of all certificates issued

Referrals —The most frequent diagnoses for which atients were referred to hospital or elsewhere were

	Proportion per 1000 total referrals	
	Male	*Female*
sychoneurotic disorders	20 2	21 2
cute tonsillitis	28 1	27 2
ronchitis	63 3	33 1
lcer of stomach and duodenum	25·6	10·6
ppendicitis	20·5	23 3
isorders of menstruation	—	31 8
ractures	23 7	10 1
aternity antenatal	—	58 5

he conditions for which admission to hospital was most ften arranged were appendicitis and pneumonia.

Number of consultations.—The average number of onsultations during the year per patient on the doctors' ists was 3·4 for males and 4 2 for females.

From these and many other findings tabulated in he report Dr LOGAN concludes that simple data of he sort recorded by the eight practitioners are suitable or statistical analysis He admits that conscientious ecording was an additional burden on the doctors , ut the weight of this, he feels, was greatest at the tart, and he believes that such a system can be kept going without undue difficulty even during busy periods. " There can be little doubt," he says, that general practitioners' records " potentially constitute one of the most valuable sources of information on morbidity " The size and scope of the inquiry may eventually be increased but meanwhile it is being continued on the same lines for a second year Dr LOGAN adds two warnings One is that terminology and measurement throughout the whole field of morbidity statistics are still being developed, and the best methods of tabulation are undecided The other is that doctors who think of embarking on their own comprehensive analysis should recognise that this is likely to prove much more burdensome than the record keeping itself Even the General Register Office, with its large resources, seems to have been quite heavily taxed in analysing the data from this limited survey

This survey was designed to show what constitutes general practice But clearly a similar approach might throw much new light on the sources, extent and effects of morbidity It is a strange twist that has brought the family doctor who prides himself on dealing with individual people to his present position in which in league with a Hollerith machine he will be handling masses of figures Perhaps this first account will give him heart for the task

Annotations

MAN AND DISEASE

THE historical record of man's early steps towards the understanding and treatment of disease may often seem to the student a jumbled and unhelpful story that is of little use to him in absorbing present-day teaching But careful study and perceptive interpretation can pick out the threads from this tangled tale and turn it into a fascinating introduction to the more familiar events of recent years. And this is what Sir Henry Cohen did at the Royal Society of Medicine last week when, in his presidential address to the section of medicine he discussed the Evolution of the Concept of Disease

Primitive man was little concerned with the nature or cause of disease he concentrated on its cure Sir Henry pointed out how the earliest remedies were based on certain doctrines which though they were crude and supernatural, had profoundly influenced later thought. There was the doctrine of similars whereby for example, stewed raven was the cure for greying hair ; the doctrine of signatures which held that distinctive markings on a plant indicated its medicinal properties (thus, yellow celandine was the thing for jaundice) ; the doctrine of analogy which drew comparisons between the treatment of animals and of man ; and the doctrine of contagion which attributed a baleful influence to external forces and which led among other things, to the popularity of moonstone for mental illness. When it came to the appreciation of the nature of disease, two ideas had dominated man s thought since earliest times : disease as a separate entity quite distinct from the individual affected ; and disease as a deviation from normal These two views had coexisted until the present day sometimes overlapping sometimes one or the other predominating according to the philosophy of the time and the influence of outstanding personalities.

The most primitive form of the " entity idea was the explanation that disease was caused by a variety of evil spirits, which called for treatment by incantation burnt offering and sorcery These practices could still be recognised from time to time in modern life : the raw potato carried for the prevention of rheumatism was the equivalent of the primitive amulet and Sir Henry recalled a case in his own experience where the relatives of an Armenian patient had sacrificed a pigeon in the belief that they might thereby instil new life into the dying woman. The notion of diseases as separate entities developed from this demoniacal concept : and it was fostered by the careful descriptions of individual illnesses recorded by Hippocrates and later physicians They all dealt with particular cases, and no attempt at generalisation was made until the 9th century A.D when Rhazes of Persia differentiated between smallpox and measles. As many separate diseases became recognised the idea gained ground and it was given impetus in the 17th century by Linnaeus s *Systema Naturae* in which he observed that there are as many species as there are diverse forms that were created in the beginning ' and by Sydenham who declared that diseases were ' to be reduced to certain and determinate kinds, with the same exactness as we see it done by botanic writers in their treatises of plants." The entity point of view reached its peak perhaps when in 1763 François Boissier de Sauvages botanist and physician (botanist first it seems) grouped diseases into classes, orders genera, and species (of which there were 2400 in all) This conventional and rationalistic outlook of A (the patient) plus B (the disease) was still apparent Sir Henry thought, in much of our teaching today It was often responsible for a misguided dependence on pathognomonic physical signs and a fondness for the penny in the-slot diagnosis

The alternative view of disease as a deviation from normal had its roots in Greece whose philosophers sought to generalise from inadequate particulars and to conceive the whole of Nature without a sufficient knowledge of its parts They developed the idea of the four humours—blood, phlegm, yellow bile and black bile—that was to dominate medicine for 2000 years But it was before the humours were described that Plato first stressed the discord of disease, attributing it to abnormal quantity quality, or position of the four elements of the body Plato s views led to the school of thought whose followers Galen called the Dogmatists and who held the field for a century after the death of Hippocrates They were followed, in the 2nd and 3rd centuries B C, by the reactionary Empirics who, though they were mainly concerned with treatment, had the idea of a syndrome And a century or so later came the Methodists who simplified everything by classifying all diseases according to the state of the pores relaxed pores called for astringents and constricted pores for laxatives, so that treatment was very simple From these early beginnings the idea of deviation from normal had to await the development of anatomy and physiology before it made substantial progress, and things did not begin to move until the 16th and 17th centuries Physics and chemistry then began to play their part in disclosing the deviation from normal, and Sir Henry particularly emphasised the significant effect on medical thought of the synthesis of urea in 1828, which showed clearly and for the first time the relevance of chemistry to medicine The discoveries of the 19th century brought increasing knowledge of the normal and departures from it, but there was still the risk of interpreting such newly recognised conditions as hyperchlorhydria, hypertension, and polycythæmia as distinct entities

Turning to the present scene, Sir Henry declared that the concept of disease as a deviation from normal should dominate our teaching and our approach to medicine The constant patterns—the syndromes or symptom-complexes—in which symptoms and signs appeared always indicated one or more of three aspects of disease its site, the associated functional disturbances, and the causative factors Specific and common patterns could conveniently be regarded as entities, but there were dangers in giving too much scope to this view, which lulled the doctor into being satisfied with a label and reduced thought to a minimum Philosophic inquiry in medicine was apt to be regarded as an arduous eccentricity for which few physicians today had either the opportunity or the inclination But it was, Sir Henry concluded, a worthwhile pursuit, for it helped to keep a balance between our dogmatism on the one hand and our scepticism and discouragement on the other Above all, it inculcated humility in the presence of great minds which was the surest shield against intellectual arrogance

DEHYDRATION IN INFANTS

THE last few years have seen rapid developments in fluid and electrolyte therapy based on physiological principles established during the past three decades But treatment by fluid replacement is over a hundred years old, for the first reported cases were treated by Dr Latta during a cholera epidemic in Scotland in 1832 [1] Progress thereafter was slow, but, following the work of Marriott [2] on dehydration in infancy, fluid replacement speedily established itself as of outstanding importance in the treatment of many diseases—and especially those producing diarrhœa in infants At the annual meeting of the Australian Pædiatric Association earlier this year the present position of this method of treatment in infants was reviewed in four papers that have now been published Macdonald,[3] dealing with the physiological principles involved in the maintenance of the fluid and electrolyte balance in infancy, emphasises the importance of using the correct terminology in discussing electrolytes But, as Dr Ennis points out in our correspondence columns this week, many clinicians do not take kindly to the milli equivalent and prefer to stick to the familiar "milligrammes per 100 ml" They are reproved for their reluctance to move with the times by Professor Dods,[4] who pointed out at the Australian meeting that "it was only by talking and thinking in these terms of chemical equivalence that they could have any real concept of electrolyte patterns Without this concept of electrolyte anatomy, any discussion of the problem must necessarily be vague and nebulous"

The electrolyte pattern of the newborn infant differs from that of an adult in several ways [5] The potassium, chloride, sulphate, and phosphate content of the plasma is higher and the bicarbonate and protein levels are lower In the premature baby the bicarbonate level is even lower than in the full-term newborn, and the tendency to acidosis that is present in all newborn babies is more definite The control of acid-base equilibrium is often unstable and the regulating mechanism of the kidney is incompletely developed Campbell [5] points out that late tying of the cord may add from 3 to $3^{1}/_{2}$ ounces of blood to the baby's circulation, equivalent to giving a 10-stone adult a blood-transfusion of $3^{1}/_{2}$ pints She advocates delayed feeding of newborn infants, whether premature or full-term, principally in order to give the babies rest. Premature babies begin to look dehydrated at forty-eight hours and Campbell advises that the administration of fluids should begin then, especially if the infant is much jaundiced fluids should be given parenterally if the infant is not taking too well by mouth In her view the high serum-bilirubin, together with low blood glucose level, may be dangerous to brain tissue and is a possible cause of "premature kernicterus" [6,7] Williams,[8] discussing the management of dehydration in enterocolitis, also emphasises that assessment can be made largely on the clinical evidence and that biochemical tests are not essential in the early acute phase The Australian recommendations for treatment are similar to those given in the recent Medical Research Council memorandum on the treatment of acute dehydration in infancy [9] One important point is that potassium depletion is likely to occur if long-continued intravenous therapy is given without the administration of potassium [10]

Finally, Stuckey [11] deals with the surgical aspects of dehydration in infancy and childhood, with particular reference to high intestinal obstruction Dehydration in these patients is due partly to the abnormal losses of intestinal secretions by vomiting, aspiration, or fistulæ, and partly to the failure to take or retain normal amounts of fluids by mouth Treatment is planned in four phases The first step is resuscitation, either from surgical shock or from severe dehydration Stuckey favours blood or serum given fairly quickly, he does not mention plasma, which is more commonly used in this country If dehydration is severe the protein-containing fluid is followed up with glucose saline solution. The second phase is concerned with the correction of moderate dehydration over the next twenty-four hours with replacement fluids, in amounts equal to 6% of the body weight, followed by maintenance fluids, in amounts up to 15% of the body-weight daily Stuckey recommends that the replacement fluid should contain potassium as well as sodium, but some may question the routine use of potassium at this stage The third phase, starting on the second day of treatment, consists in making up any deficit and in maintaining fluid and electrolyte balance On the third and subsequent days the balance is maintained and protein or amino-acids are given Throughout a constant check is kept on all fluid losses so that the balance can be carefully regulated

The chief lesson seems to be that effective treatment, derived from sound physiological principles, can be given without recourse to expensive, and often unobtainable, biochemical assistance

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THE BLIND IN OUR MIDST

AN increase in newly registered blind persons from 586 in 1948 to 11 155 in 1951 is revealed in a report y Prof Arnold Sorsby[1] The bulk of the new registra ons now come from the oldest age group ; but clearly e extension of welfare services, and greater readiness patients to seek certification and hence of doctors certify borderline cases have also played a part.

Cataract, glaucoma, and senile macular degeneration gether, now account for 50 7% of all cases of blindness 1950, as many as 80% of cataract patients are reported not having had treatment. This seems deplorable a time when advances in the technique of cataract traction have made the operation, in expert hands, fer and more widely applicable than in the past. he matter certainly calls for further inquiry The roblem of glaucoma is less tractable, principally because the insidious course of the disease in the ageing he disease may be halted in its early stages by timely peration and thus prompt detection is of the greatest nportance. The growing number of glaucoma clinics association with eye hospitals is a token of medical wareness of this problem. More such cases are likely come under medical care at an operable stage when e supplementary eye service is superseded by the ermanent service

FITNESS AND HEALTH

AT Leighton Park last Saturday Sir Russell Brain R C.P., opened a big new gymnasium which forms part f the school's war memorial What, he asked is the lation between fitness in the everyday sense of keeping t and fitness as the biologist uses the term when he peaks of survival of the fittest ? Fitness to survive epends on changes that give an organism increased ontrol over its environment but all creatures alive oday must have passed this survival test Man, the ger and the typhoid germ all equally come within the iological definition of fitness ; and though man may egard himself as of more value than a typhoid germ hat after all is only his prejudice

It is obvious, continued Sir Russell that health has layed and is still playing a major part in evolution : o be fit (in the full or ideal sense) is surely to be able to ake the best possible use of one's capacities, both hysical and mental—which in biological terms means eing as fully adapted as possible to one s environment. What then is health ? In its negative definition it is the bsence of disease But disease is itself a negative term neaning the absence of ease Can we then define health s the absence of the absence of ease ? To do this is ot only to go round in a circle but to make health and lisease look simpler than they really are. The *Nomen lature of Diseases* itemises 15,000 ways of being ill ; no loubt others are waiting to be discovered and the more e understand of these diseases the more complex we ind them In the case of many infections for example t is true to say that whether a person catches them or ot depends on a long chain of circumstances many of which are entirely outside his control There is not some ingle condition called health which has magic properties which make people immune to every kind of illness The prevention of disease depends first on knowledge and then usually on the coöperation of numbers of different people in different spheres of life—including of course the potential patient

"But I am afraid that the part the potential patient can play is, on the whole, rather limited, and what are sometimes called a few simple rules of health, however desirable they may be in themselves, and however they may promote a sense of well-being have on the whole very little to do with the prevention of the majority of diseases. It follows that anyone who propounds some simple way of maintaining health, and preventing all or a large number of diseases, receives no support from science "

Turning to health of mind, Sir Russell agreed that we live in one of those epochs when human culture suddenly undergoes a rapid change But stress of life is insepar able from living it is part of the evolutionary process Our problem is how to adapt ourselves to new ideas and modes of living and how to face emergencies which may threaten both our individual existence and our civilisa tion This is not a problem to which medicine, as such can give any answer The doctor may make the diag nosis but the stresses of modern life are part of the culture to which he himself belongs, and any possible way of dealing with them must reach out far beyond medicine and concern itself with a belief about ultimate things on which doctors differ as much as other people Offering what was therefore a personal rather than a medical view Sir Russell pointed out that happiness contributes to peace of mind and therefore to health of mind and health of body ; and on the whole the happiest people are those whose work is of such absorbing interest that for them there is no great distinction between work and play He believed too, that the nature of man is such that his happiness is closely related to the life of Nature and the cultivation of the soil : I suspect that in any society there is a certain critical balance between agriculture and industry, and when the balance is tipped too far in the direction of industry some virtue goes out of the society " And finally there is the spiritual isolation of modern man

> Cut off largely from the rhythms of the earth, from the natural ties of the small community from conscious communal efforts, and from the secular and religious festivals in which the individual and the community alike found expression and satisfaction for their deeper feelings, modern man experiences a spiritual hunger of the nature of which he may be hardly aware Perhaps one thing which made the Coronation ceremony so moving was that it momentarily satisfied this deep human need. Here I believe is the cardinal problem which modern society has to solve if men and women are to be able to cope with its inevitable stresses.

But the view of health as the absence of disease of body and mind is very incomplete : it is not enough not to be ill—even not to be ill in 15 000 ways We must make it our aim that everyone should have the best oppor tunities for the fullest possible development and use of both his body and his mind. This idea of positive health (sometimes claimed as a modern discovery) is, like the word gymnasium ' as old as Plato—who thought that one of the virtues of gymnastics was that it kept the doctor away though he admitted its impotence against what he called "an attack of illness incidental to the time of year ' In the gymnasium people learn endurance control, and (issuing from that) poise or balance and we know by experience, as Plato knew, that training in these bodily virtues develops them also in the mind.

Man is regarded as supreme among animals because his nervous system is by far the most complex reflecting the enormous range of his interests and activities and if it is argued that the tendency of evolution is to produce creatures which react to an ever wider and richer environ ment, then man represents the highest point so far reached. But can we assume asked Sir Russell, that contact with a complex environment is in itself a good thing ? The amœba might well defend the simple life ! To what environment, then is man required to adapt himself ? More and more people would now say that all there is for him to adapt himself to is the material world, as analysed measured and calculated by the scientists ; but future historians of thought may be surprised at the long acceptance of this materialist philosophy by so many intelligent people If the material world is all, there can be no basis for lasting values independent of material forms, but if it is not the whole story, at least the door is opened for exploration of a realm in which such values could exist One form of life or mode of living cannot be regarded as better than another unless values exist which transcend the laws which govern the behaviour of matter If so, as Walter de la Mare says

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[1] The Causes of Blindness in England 1948–1950 Report by Prof. Arnold Sorsby H.M. Stationery Office. 2s

> "Two worlds have we, without, within,
> But all that sense can mete and span,
> Unless it confirmation win
> From heart and soul, is death to man."

This means, said Sir Russell, that health, valuable as it is, cannot have top priority it must often be sacrificed for some greater end, and some of the greatest servants of mankind have not only triumphed over illness but have somehow made their sufferings serve a higher purpose He ended his address by saying

> "Health, if you like, is a means to fitness, but fitness—for what? I leave that question with you as I declare open this gymnasium, dedicated to fitness of body and mind and to those spiritual values for which those whom it commemorates gave their lives"

HOSPITAL COSTING

THE Minister of Health has set up a working party to devise a practical system of departmental and unit costing in hospitals, on the basis that subjective accounting will be retained This action arises from consideration of the reports on costing by King Edward's Hospital Fund for London and the Nuffield Provincial Hospitals Trust,[1] and also the second report on costing of a subcommittee appointed by the Committee of Regional Hospital Board Treasurers Mr W O Chatterton is chairman of the working party, which includes representatives of the Ministry, the administrative and financial officers of hospital authorities, the King's Fund, and the Nuffield Trust The working party, which is being asked to complete its task, if possible, in six months, will be free to suggest different systems for different types and sizes of hospitals

COLD-STORAGE OF LIVING CELLS

Thomas Alva Edison is reported to have said "Invention is ten per cent inspiration and ninety per cent perspiration" This description is particularly appropriate to the invention of methods of preserving living cells in the frozen state The idea that animation might be suspended indefinitely has often inspired attempts to preserve cells at low temperatures Success was rare because of the particularly destructive effects of the act of freezing and because it was not realised that each type of cell required an individual technique of freezing It was discovered in 1949[2] that death on freezing could be avoided if the cells were suspended in a medium containing glycerol, and this removed at one stroke the main barrier opposing the preservation of living cells in the frozen state The importance of the discovery has been shown by the astonishingly rapid progress in the last four years, which was reviewed at the Royal Society of Medicine on Oct 27

The use of glycerol to preserve frozen yeasts, protozoa, red blood-cells, spermatozoa, and even organised endocrine tissue was surveyed by Dr Audrey U Smith Adverse effects, such as thermal shock and the differences between cells in their permeability to glycerol, make necessary individual techniques of freezing for each type of cell and tissue The mechanism of the protective action of glycerol appears to be clear cut and simple[3] According to Dr J E Lovelock the most serious and unavoidable source of damage on freezing is the rise in concentration of the electrolytes of the cell and its medium Glycerol prevents this excessive increase of salinity, which is otherwise unavoidable when water is removed as ice during freezing

Skin is a complex mixture of cellular types, and the development of a method of freezing and storage which harms none of them is a considerable achievement We have already commented[4] on the success of Billingham and Medawar[5] in storing rabbit skin without loss of function for one year at −78°C In describing this and other experiments on the preservation of skin, Prof P B Medawar, F R S, emphasised the singular lack of toxicity of glycerol Its effectiveness as a preservative must depend greatly on this property, for during freezing it displaces much of the water within the cell

The successful transfusion of human red blood-cells after long storage at −78°C is an accomplished fact[6] To freeze and store a few bottles of blood at this temperature is fairly simple, but to freeze a blood bank to this temperature would be a major engineering problem Washing of red blood cells after storage, to remove glycerol, is also no simple matter when large volumes of cells have to be treated Progress towards the solution of these practical problems was discussed by Dr P L Mollison An account of the successful transfusion of red blood-cells after three months' storage at −20°C was particularly encouraging If blood can be kept at this temperature large-scale storage of frozen blood may soon be feasible

DISHARMONY IN HYBRIDS?

THE family doctor is from time to time consulted about a proposed inter-racial marriage There may be serious risks to many such marriages from the different social backgrounds of the partners, but there are also often held to be risks that the children may show disharmony of physical growth Trevor[7] has assessed and analysed all the information he could find on physical measurements of racial hybrids In many ways this information is deficient the original parents, living perhaps 300 years ago, were of course not available for measurement and some related family group had to be measured instead, the techniques of measurement used are not always clearly stated, and the composition of the two parent races is not always as clearly known as in the Norfolk Islanders, who are more or less equally derived from English seamen from the *Bounty* and Tahitians But certain general conclusions emerge Thus for nearly every character the mean values for the hybrids lie between those for the two parental races, the distribution of measurements round the mean is approximately normal and shows no signs of bimodality, and the variation shown by the hybrid group is (surprisingly) not much, if any, greater than that of the parental races There is, then, no reason to expect disharmonious skeletal growth in the children of inter racial marriages

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THE Nobel peace prize for 1952 has been awarded to Dr ALBERT SCHWEITZER, who for many years has worked as a medical missionary in Central Africa.

THE next session of the General Medical Council will open on Tuesday, Nov 24, at 2 P M, when Prof DAVID CAMPBELL, the president, will deliver an address. The Medical Disciplinary Committee will meet on Wednesday Nov 25, at 11 A.M

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[1] See *Lancet* 1952 ii 1067

[2] Polge C, Smith, A U Parkes A S *Nature Lond* 1949 164, 666

[3] L[illegible] J E *Biochim biophys Acta* 1953, 11, 28

[4] *Lancet* July 4 1953 p 26

[5] Billingham R E, Medawar, P B *J exp Biol* 1952, 29, 454.

[6] Mollison P L Sloviter H A *Lancet* 1951 ii 862.

[7] Race Crossing in Man The Analysis of Metrical Characters By J C TREVOR, PH D lecturer in anthropology, University of Cambridge Eugenics Laboratory Memoirs, XXXVI London Cambridge University Press for the Galton Laboratory 1953 Pp 45 12s 6d

Special Articles

MAKING THE MOST OF PRESENT RESOURCES

SECOND HEALTH SERVICES CONFERENCE *

THE first conference of the Institute of Public Administration was held 2¼ years ago and at that time everyone agreed that what was needed in the National Health Service was more coöperation Mr HENRY LESSER, who took the chair at the second conference, held in London on Oct 28–30 remarked regretfully that no general pattern of coördination has emerged The popularity of the service with the public is beyond question, but the increasing cost, however is giving rise to anxiety There are two ways of using resources to the best advantage (1) by ensuring that the structure of the service is good and (2) by raising the standard of day to-day management

FINANCE IN THE DEPLOYMENT OF PRESENT RESOURCES

Mr LESLIE FARRER BROWN (secretary of the Nuffield Foundation) recalled that of the £500 million we spend on the N H S, 60% goes to the hospital service, 30% to the practitioner services, and 10% on the rest or breaking it down another way, 60% goes on wages and salaries and 40% on materials. The increases have been mainly in salaries and wages partly in increases of staff and salaries and wages must always be the chief cost Inevitably we have to ration our resources no country can meet all the potential medical needs of its people. If we think that £x million should be spent on the general practitioner service we must be ready to suggest what else can be cut down to allow for it. The quality of personnel is of the first importance for judgments are made by people and better judgments will be made by better minds supplied with better information and spurred to achieve better results We must study scientifically the ways of doing things, and pass on the knowledge gained to those working the service We must also make up our minds he said, whether we want decentralisation of authority or more centralisation for the present compromise is most unhappy

Prof R M TITMUSS (professor of social administration in the London School of Economics) said that resources are being wasted because of factors outside the health service If we take no steps to control road accidents we must expect more demands on casualty departments. If we insist on building 2 bedroom houses we must expect to give more custodial care to the aged sick Little thought is being given to these preventive factors We are concentrating more today on getting the general practitioner into the hospitals than into the local community service A small London investigation into the use made of the social services by people over 70 living alone revealed that only 1 in 40 of them had learnt of these services from their general practitioners: they had usually learnt of them from neighbours, friends or conversations heard in buses The highest demands on the services of practitioners and hospitals comes from a relatively small group of the public—from the aged the disabled, the victims of road accidents, mentally sick adults, and emotionally disturbed children If preventive work could reduce the demands for treatment from this group then the costs of the service might be reduced by as much as 20% We *must* integrate the family doctor with the local welfare services. From the medical staffs of hospitals we need a greater sense of personal responsibility and a greater loyalty to the whole purpose of the hospital rather than to their own specialty

Mr J C DAVIES (chairman of the Fountain group of hospitals) believed that every organisation could be more economically run and advised members of all committees not to concern themselves merely with things in the process of change—which are naturally brought to their attention—but also with the things which are continuing and therefore apt to go unscrutinised Cost-accounting allows comparisons to be made not only between one hospital and another, but also between costs in the same hospital at different periods. If a hospital could use the money it saved for other purposes within its own economy there would be more incentive to save and he suggested that the service needs an economy salesman, to point out the rewards of thrift.

Mrs. ORMEROD speaking from long experience gained on hospital management committees, agreed that there has been a decrease in social responsibility among medical members of hospital staffs, though when they and their wives had to raise money for the voluntary hospitals they responded splendidly They are also reckless in the use of woman power in the form of nurses almoners, and record clerks Mr C S BANGAY (clerk to the London Executive Council) thought the partition of the service under three heads makes agreement harder to arrive at than a truce in the Far East. He favoured the establishment of a central coördinating body and the removal of the Ministry of Health from the service

Mr GEORGE WATTS (secretary of the Oxford Regional Hospital Board) suggested that hospitals should allocate a small sum to research into methods of work on their own premises One such survey in a general hospital had already pointed the way to possible savings; and the Oxford R.H.B were consulting industrial experts about economies in the laundry and catering departments.

Other speakers emphasised the need for a common method of financing all parts of the service the economies to be hoped for from prevention of disease and better health teaching the importance of good food and the great cost to the country from road accidents and accidents in the home In replying Mr FARRER BROWN confessed to favouring removal of central control from the Ministry of Health and giving it to an all purposes health board, with subsidiary health boards at regional and local levels.

DOMICILIARY AND OUTPATIENT SERVICES

Dr A LESLIE BANKS (professor of human ecology at Cambridge) spoke of the changing pattern of disease in our time and the shift towards middle and old age in the hospital population Our investigation services, he said, have nearly reached saturation point, and the rapid turnover in the wards is a strain on the inpatient services Much investigation formerly done in the wards is now done in the outpatient department and more could be done there if quarters were not cramped and if the special departments added to the hospital when the pace was slower could cope more quickly with the work reaching them At present they are bottlenecks wasting time and money Lack of adequate appointments systems also wastes time—the patient's working time—and loses us money The time of general practitioners, too is wasted unless they can get speedy reports from special departments He thought that before extending the domiciliary services we should improve those we have, improve outpatient facilities and train a corps of administrators to deploy our resources better

Dr KENNETH COWAN (M O H for Essex) said that the right person to deploy our domiciliary resources is the general practitioner; and he needs to know what they are The local authorities should make their services readily available the Government provides help and money for the disabled and there are vast voluntary services not used to their full extent He thought it strange that little has been done to provide a domiciliary geriatric service comparable to the geriatric service now provided in hospitals for the chronic sick Plenty of trained nurses could be found to look after postoperative patients in their own homes Domiciliary midwives are often unemployed while hospital maternity beds are full There are thus many resources which administrative bodies are failing to use Regional surveys might be made of special problems, and of facilities for dealing with them

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* The programme and papers of the conference have been printed by the Institute of Public Administration, Haldane House 76A, New Cavendish Street London, W 1

Dr A BEAUCHAMP (vice-chairman of the Birmingham Executive Council) thought postoperative pre-convalescent patients might certainly be nursed at home, provided the home is suitable The general practitioner knows, and can—if asked—report on, the home He suggested the reorganisation of outpatient departments If appointments systems were used, the space wasted on outpatient halls could be used for other purposes The patient who comes at 9, when the consultant is not going to turn up till 11, has not only a long wait but a *worrying* wait, and it is bad for him. Mothers should be encouraged to have their babies at home our midwives are first class, our home help service getting better and better To deliver a mother in hospital costs the country £40 for a fortnight's stay Again, we are not teaching people to live healthily when we herd them into overcrowded houses in a smoky atmosphere

Other speakers mentioned the failure of some hospitals to inform the general practitioner when a patient leaves hospital

Dr A TALBOT ROGERS, chairman of the General Medical Services Committee of the B.M.A , thought the general practitioner should use the outpatient department for purely consultative purposes, and the patient should come back to him when the consultant has reached his diagnosis Sometimes patients go on attending for months, perhaps so that a keen registrar can watch their progress It is right that a patient should be seen again after an operation, but it is not right that the outpatient department should take over what the family doctor ought to be doing

Dr G M WILLIAMSON said that in Leeds they have formed a general-practitioner-hospital relationship committee which has already done grand work Moreover, the geriatric committee of the regional board moves round the area and holds conferences, each lasting a day, with general practitioners, medical officers of health, and all others interested This practice has been much welcomed

A surgeon said that what he and his colleagues used to think of as "our hospital" was now one of a group, with its administrative centre six hours' journey away In defence of his brotherhood he added diffidently that he was punctual, wrote his letters, and kept a social dossier of every patient he saw Dr R I MACALLUM (Newcastle) also spoke well of the punctuality of surgeons, and reported on the good success of an appointments system so arranged that the consultant was able to see up to 20 new patients by a certain time

In reply, Professor BANKS noted that the discussion put the general practitioner right in the centre of the picture There is nothing radically wrong with the service, but we want, he said, three things we want to know how much we can spend, we want the best administration we can get at the local level, and then we want to leave the damned thing alone for five years

THE WHITLEY SYSTEM

Mr K J JOHNSON (a member of the ancillary staffs Whitley Council), in his printed contribution, explained that the Whitley Councils are made up of two sides, one representing employers, the other employed Decisions are reached by agreement of both sides, there being no voting *between* the sides, though there may be voting *within* the sides Failure to agree leaves both sides free to seek arbitration He said (at the third session of the conference) that he represented the employer's point of view The decisions of the councils are often shown to result in anomalies of pay and conditions, and the machinery is said to take an unconscionable time to work, but while he agreed that these allegations are true he thought the work of the councils must be judged as a whole and that it would be difficult to speed it up One cause of delay, he believed, is the too common appeal to arbitration Many of the appeals are trivial, even frivolous He criticised the composition of the [illegible] side Organisations which are already [illegible] on it are naturally not willing to cede places to any new organisations which may be formed, so these sometimes find it very difficult to get representation Again, both sides of the council ought to have [illegible] responsibility for the conduct of the service, but it happens that the employer side have to be responsible for the cost, while the employee side have to put the interest of their members first. The agreements of the councils are thus nearly always a compromise, and should be accepted as such

Dr JOHN GIBSON (formerly medical officer of [illegible] for Huddersfield) wished to see better coördination [illegible] results It should not be possible for a nursing orderly to receive, in some circumstances, more pay than a State-registered nurse working the same hours Nor is it reasonable that a non-resident nurse working [illegible] than 40 hours a week should get her meals and uniform free, whereas if she works more than 40 hours she has to pay £30 a year for them Nevertheless, negotiating machinery is necessary, and he hoped to see the weak spots in the Whitley council system strengthened.

Mr S G HILL (superintendent of the General Hospital, Northampton) agreed that there were anomalies but added that, in the health service, posts with the same name might vary very much in the demands they make on the officer holding them He thought there was a case for making some posts "non-Whitley" He agreed that new employee organisations tend to be unrepresented on the councils

Mr BANGAY (clerk to the London Executive Council) deplored the lack of knowledge of conditions on the management side The fact that the representatives on the employee side are all men may explain, he said why women in the third grade get less money than men in the first grade He suggested that some arrangement allowing for merit awards would be helpful. The idea was treated sympathetically by other speakers Several, too, agreed with him that the employer side is often not well informed about conditions of service

A speaker from the mental hospital service rated the councils with both humour and good humour for their dilatory behaviour, which, he said, is causing the wastage of 80% of mental nursing recruits and accounts for a deficit of 20,000 female and 8000 male nurses in the mental hospital service At present one girl often has to look after 55 acutely ill mental patients A male nurse, after qualifying, works for 9 years before he gets as much pay as a resident ward orderly, and a female nurse may work 8 years as a staff nurse before she gets a staff nurse's pay

Sir ARTHUR HOWARD, chairman of the Whitley Councils, defended them as well as he could the people who serve on them are not perfect and may not always make perfect decisions there will always be anomalies but the object is to satisfy members of the health service that they are getting justice, and in the main the councils are working well Subsequent speakers mentioned several striking anomalies, and Mr Johnson in replying, summed up the rather disgruntled [illegible] of the meeting when he said that if the Whitley Councils did not represent an ideal hole, he at least didn t know of a better one.

USING MAN POWER TO THE BEST ADVANTAGE

In the absence of Mr H A GODDARD, who lately directed the *Nursing Job Analysis Enquiry* for the Nuffield Provincial Hospitals Trust, the third session was opened by Mr P H CONSTABLE (house governor to St. George s Hospital) Over 60% of the cost of the N H S., he said, goes on man power some of which is wasted in coping with obsolete buildings We have too long based our policy in hospitals on opinion instead of facts. The nursing job analysis has given us facts some of which are disagreeable Many people find it hard to believe, for instance, that the end result of nursing is administration. He quoted a *Lancet* editorial which summed up the position "The student nurse is so little of a student and so much of a nurse for the same reason that the sister is so little of a nurse and so much of a clerk. Similar job analyses are needed, he said in every branch of the hospital service. He suggested that the hospitals might themselves finance such studies

Sir ZACHARY COPE (chairman of the Medical Recruitment Committee, 1953) advised using our facts with discrimination We should gain some useful information, he thought, if hospitals would compare their volume of work, and the numbers of their staff, in—say—1938 1946 and 1953 Such a comparison would show whether there had been too great an addition to cost, and could be made more cheaply than a job analysis He mentioned Mr Goddard s opinion that we have enough nurses to man all our hospital beds if they were properly distributed. But it would be hard to distribute them properly without direction, and rather than direct we must induce—by offering special advantages in those fields where they will not work at present. In outpatient departments, 75% of the work done by nurses could be done equally well by chaperons He thought the medical staff would be intolerant of job analyses. The N.H.S has inherited from the voluntary system the custom of appointing a consultant to several hospitals, often far apart, so that he travels long distances Man power would be saved if in future, doctors were appointed to hospitals nearer their homes. Appointments systems, though laudable have the drawback that they allow the consultant to limit the number of new patients he will see at a session and some doctors are so conscientious about examining their patients that they find they can only see 3 or 4 In the old days the consultant saw all comers. Mr Goddard, in the paper printed and circulated to the conference, said that the visiting teams of consultants sent out to hospitals by the Ministry could not expect in the time at their disposal to find out facts as effectively as a job analysis. He has taken part in the work of such teams and believes they can be quite effective.

Miss HELEN M. KEYNES (St. Ebba s Hospital Management Committee) had found doctors ill company on committees because, she said they seem to want to upset the committee and run the hospital themselves. Some other speakers seemed to have had similar experiences.

A member of the Scottish Dental Association said that neglect of children s teeth under the N H.S means increased expenditure later Mr A. ASHWORTH (Mansfield) deplored the General Nursing Council s policy of subordinating every other consideration to the student status of the nurse thus making it very difficult for some hospitals in the provinces to staff their beds Miss F F LILLYWHITE (G N C) pointed out that the Council is charged with the training of nurses and not with the staffing of hospitals; but Sir Zachary Cope rejoined that it is impossible in this instance to consider training apart from staffing

Mr W S WILKINSON (Secretary, Pharmaceutical Committee, London) mentioned the delays patients suffer because people will not take the responsibility for making quite trivial decisions—illustrating his thesis from the story of a prescription for a baby's truss which did not happen to be of the authorised size He also pointed out how much time busy people nowadays spend on committee meetings, and on travelling to and from them Here he said is another field for scientific study Mr COLIN ROBERTS (North Liverpool Hospital Management Committee) spoke of the saving possible on domestic work in hospital if the domestic staff are taught how to use the labour saving devices provided, and if their health and welfare are supervised.

Mr JOHN GRANT said that doctors employed in a hospital should not be appointed to the board of that hospital This remark brought more applause than any other at the session—to the disappointment of Sir Zachary who had never encountered any friction on his hospital board over forty years. Mr Grant and other speakers favoured further job analyses in hospitals Dr GLYN HUGHES saw the force of not encouraging consultants to work too many sessions at hospitals too far apart, and thought that when the journeys became a burden to him some of the older man s appointments should be transferred to younger men Nevertheless he thought it was important for general practitioners to keep the link with hospital consultants which such sessional visits provide He agreed that outpatient departments should be used for consultative purposes, not for long term treatment. He believed the visiting teams from the Ministry can do a good job

Mr CONSTABLE, in replying remarked that the G.N C do in fact, give very careful consideration to the difficulties of provincial hospitals over recruitment of nurses

THE DRUG BILL

In a paper on the Medical Profession's Contribution to Economy in Prescription and Treatment Dr A M G CAMPBELL (consultant physician to the United Bristol Hospitals) pointed out that the increased cost of prescribing could not be attributed solely to the fact that the State paid the bill for the actual cost of drugs and dressings had risen fantastically during the past few years. In hospital the largest single item on the drug bill was antibiotics At the Bristol Royal Hospital an economy committee, consisting of 5 members of the staff, including the pharmacist reviewed expenditure each month and they were trying to instruct residents and students in the economical use of drugs, especially antibiotics. They had installed diagrams and charts in the wards, showing the effective range of the drugs and pointing out their abuses and members of the staff had helped in the preparation of a small booklet [1] on the use of antibiotics On the question of proprietary and non proprietary preparations, Dr Campbell said that it was quite clear that in many preparations the *B.P* compound was just as good if not better than the proprietary one and very much cheaper In Bristol the hospital pharmacists had been asked to dispense wherever possible, *B.P* drugs instead of proprietary preparations, unless specifically ordered by the consultant Dr Campbell suggested that the College of General Practitioners could profitably examine the question of economy in the use of drugs and he hoped that the college would include in its plans for research trials designed to compare the results obtained with proprietary and non proprietary drugs

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[1] See *Lancet*, 1953 i, 837

Dr Campbell was unable to attend the conference to present his paper, which was introduced by Dr H L GLYN HUGHES (senior administrative medical officer of the South-East Metropolitan Regional Hospital Board) Dr Glyn Hughes thought that a consultative outpatient clinic should remain consultative and that the patient should not be referred to the hospital dispensary for his drugs

In the matter of proprietary drugs, Mr J C HANBURY (vice chairman of Allen & Hanburys Ltd), who opened the discussion, favoured a compromise between an absolute ban and a continuation of the present state of affairs If non-proprietaries alone were permitted, many firms with low overhead charges, but not necessarily the best facilities for preparing drugs, would enter the market with cheap non-proprietary compounds These might satisfy the letter of the law, but they could not be produced with that careful regard for detail that often had considerable effect on the ultimate therapeutic efficiency of a drug

Dr STANLEY THOMAS (a member of the Medical Practices Committee) disagreed with Dr Campbell's view that the G P was influenced by postal advertisements to a greater extent than his hospital colleagues Dr Thomas had had letters from consultants which showed that he and they were receiving inspiration from the same piece of blotting-paper

Dr W D HOOD (senior medical officer, Department of Health for Scotland) thought that hospital pharmacists had a considerable part to play in the planning of more economical prescribing, and he suggested that their views should be sought more often

Dr TALBOT ROGERS said that though G.P s were now being told something about the cost of prescribing they still did not know whether they were keeping in step with their colleagues in the same area The General Medical Services Committee had asked for the restoration of areal averages, which would enable doctors to see how their own prescribing costs compared with the average for the area But the work of pricing N H S prescriptions had been considerably in arrears and it had not been feasible to undertake this additional task The situation was now improving and it should be possible to start preparing areal averages next year The intelligent use of these averages and the list of comparative costs that had lately been sent to G P s would be a considerable help in reducing the drug bill

REGIONAL PLANNING

In his discussion of Medical Planning in the Regions, Sir FRED MESSER, M.P (chairman of the Central Health Services Council), made some controversial proposals which drew surprisingly little return fire The Ministry of Health, he declared, should not run the National Health Service there should be a National Health and Welfare Board, something along the lines of the Central Health Services Council This board should have the over-all responsibility for the administration of the service Hospital regions should be reduced in size, and regional boards should have authority over hospital administration Combined action by regional boards and local health authorities was often hampered by the present geographical arrangements, and it would be a great help if the regions were reconstructed to conform to the boundaries of a group of local authorities Sir Fred also proposed the inclusion of teaching hospitals in the regional service , and he was anxious that the ambulance service should come under the control of the regional boards and not the local health authorities as at present Since the start of the service, medical planning had progressed, but not in all sections of the service The emphasis had been on the hospital service and not enough attention had been given to the preventive side

Dr T LLOYD HUGHES (senior administrative medical officer of the Liverpool Regional Hospital Board) believed that regional planning had largely justified the claims that had been made for it, though certain circumstances still prevented the system achieving the benefits of which it was potentially capable Among these circumstances he included the lack of unity, which was the result of the service's division into three parts, and the shortage of nurses and doctors, particularly of doctors for junior hospital jobs

Dr T A MORRISON (chairman of the Bright executive council) put the point of view of the G P He thought that regional boards might be thinking in terms of hospital units that were too large , there was perhaps a place for smaller hospitals where the G P could treat his patients himself under the supervision of a consultant He was critical of the school and antenatal clinics of the local health authorities , nothing was done there that the G P himself could not do

Sir Fred Messer had referred to the difficulties that had arisen in coördinating the various parts of the [illegible] while its present structure was retained, and Sir ALLEN DALEY (formerly M O H for the county of London) took up this point In his view these difficulties were due more to lack of time than lack of inclination on the part of those who were helping to run the health service There was certainly not an unlimited number of people able to give time to committee work, and more and more tasks became heaped on the willing horse He agreed with Sir Fred that the present hospital regions were too few and too big , a teaching hospital should be associated with every region, but it need not necessarily be within the boundaries of the region

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International Congresses

PÆDIATRICS

THE Seventh International Pædiatric Congress held in Havana from Oct 12 to 17 It was preceded by the 22nd annual meeting of the American Academy Pediatrics in Miami from Oct 5 to 9, to which the European pædiatricians attending the in congress were invited

The congress followed the usual system of pl sessions and round table conferences , and there was an excellent scientific exhibition, in which the displays on nephrosis, epilepsy, mucoviscidosis, and tuberculosis were especially notable The plenary sessions were devoted to epilepsy, congenital heart disease susceptible of surgical treatment, prematurity, the complications of primary tuberculosis, and problems of metabolism and nutrition

The paper by Prof STANLEY GIBSON (Chicago) on Eyes, Ears, and Hands in the Diagnosis of Congenital Heart disease was a masterpiece of clinical observation and Dr HELEN TAUSSIG's review of the operations performed at Baltimore was on an equal plane

Prof CLEMENT SMITH (Boston) discussed the "hard core" of the mortality among premature infants, Prof ALAN MONCRIEFF gave a graphic account of the changes in the care of premature infants during the past twenty years

In the session on tuberculosis it was encouraging find that more and more authorities are abandoning intrathecal treatment in tuberculous and other forms of meningitis, and that isoniazid has worked greater miracles in childhood tuberculosis than it has in adults Dr EDITH LINCOLN (New York) discussed the effects of chemotherapy on the prognosis of primary infection and Dr BERNARD SCHLESINGER described the local complications of the primary complex

Of the twenty round tables the most popular appeared to be those on nephrosis, hæmatology, allergy, and liseases. Professor Moncrieff was a member of the panel n respiratory diseases of the newborn, and Prof Wilfrid Gaisford (Manchester) of that on B C G

The congress was well attended nearly two thousand nembers from 47 countries, were present.

The next congress, in 1956, will be in Copenhagen

NEOHIPPOCRATIC MEDICINE

FOUR hundred physicians from all over the world took part in the Second International Congress of Neohippocratic Medicine held at Evian in the first days of September

The congress began with the reading of the opening address of the president, Prof M H LAIGNEL-LAVASTINE Paris) who unfortunately was prevented by illness from being present. In his address Prof Laignel Lavastine pointed out that the term neohippocratism' coined by A. P Cawadias in 1919 did not signify a return to Hippocrates but an attempt to combine the scientific analytical approach predominating in contemporary medicine with the synthetic holistic, and constitutional approach of Hippocratic medicine

The following conclusions were reached by the congress

1 Internal medicine and thus the internist must take a preponderant place in medical practice Specialties are necessary on account of developments in technique, but as disease is a total ' psychosomatic " reaction, synthesis between the parts and the whole is necessary for a precise diagnosis.

2. Clinical observation must be reinstated as the most important factor in medical diagnosis because only clinical observation and the clinical critical spirit allows the understanding of the patient as a whole and thus laboratory signs are to be interpreted in the light of clinical observation

3 Consideration of the constitution of the psychophysical personality of the patient, and his physical social and historical environment independently of his disease is of the greatest importance in diagnosis and treatment

4 Parallel with the specific methods of treatment indicated by the particular disease and developed in modern medicine the constitutional Hippocratic methods adapted to the constitution of the patient, independently of his disease should be applied.

A great part of the success of this meeting was due to the untiring energy of the secretary general Prof Pierre Delore of Lyons.

Parliament

Operations on Animals

IN the House of Lords on Oct. 27 Lord STAMP moved the second reading of the Protection of Animals (Amendment) Bill. He said he realised that obviously the measure could not go any further in the expiring session but he hoped that the Government would take it up and give it their support in the new session or failing that a private member would reintroduce it. The main object of the Bill is to bring up to date the law concerning the use of anæsthesia in operations on animals [1] Lord CARRINGTON joint parliamentary secretary to the Ministry of Agriculture said that while the Government supported the Bill in principle, they could give no undertaking that they could find parliamentary time to take it up

QUESTION TIME

National Service Medical Boards

In answer to a question Sir WALTER MONCKTON Minister of Labour said that he had visited a number of National Service medical boards, and had had discussions with chairmen of other boards and officials and had attended meetings of chairmen in all regions. These investigations had satisfied him that the medical men who comprised the boards were fully alive to their responsibilities Nevertheless some errors in grading had occurred. Special investigation of cases brought to his notice, including those raised by hon. members since the end of June last, had revealed about 20 such cases which was not a large number in relation to an annual rate of about 300 000 examinations. The most common factor resulting in a man being placed in too high a grade was the failure on the part of the man to disclose his full medical history; unless a man disclosed his full medical history the board conducted his examination at a disadvantage To correct this source of error the notice summoning the man had been revised and now advised him to bring to the board medical evidence of any past disabilities and ailments.

In a few cases there had been a lapse on the part of the board in applying the proper medical standards, and in other cases there had been clerical errors. The remedy for such mistakes was patient and constant attention to detail by the medical boards when applying the standards laid down. To help towards this the chairman would be relieved of any non medical work which might be a distraction. To provide a further safeguard against errors, in future every man summoned to a medical board would be informed by notice that if he had reason to think that he had been given a wrong grading he might appeal in writing within fourteen days enclosing with his appeal any medical evidence he might desire to submit Such appeals would be referred to the regional medical officer of the Ministry of Health for advice whether medical grounds existed to justify re-examination. Ordinarily any re-examination would be undertaken by a different board Sir Walter added that nothing he had said should be regarded as a reflection on the manner in which the general body of chairmen and members of medical boards had performed their duties Their task was not easy and he could assure the House that they had maintained the high tradition of their profession.

In answer to further questions Sir Walter said he was keeping this matter constantly under review He had not stopped examining cases and causes and would not hesitate to take what action he thought right. But in spite of the publicity the number of avoidable errors was very small

Food-poisoning

Replying to Dr BARNETT STROSS, Mr IAIN MACLEOD the Minister of Health said that 300 outbreaks of food poisoning in England and Wales had been notified to him between Jan 1 and Oct. 21 1953 by medical officers of health The number of people affected according to the causal organism, type of food, and the place was as follows:

	Outbreaks	Persons affected
Causal organism		
Salmonella group	117	2309
Staphylococci group	01	2118
Cl. welchii	11	461
Miscellaneous	14	134
Unknown	97	951
	300	5966
Type of food:		
Meat and meat products	109	*605
Fish and fish products	1*	75
Duck eggs	12	15
Milk and milk products	20	1775
Miscellaneous	15	58
Vehicle of infection not established	133	1438
	300	5966
Place of outbreak:		
Hotels, catering establishments, &c.	24	29*
Schools	25	1970
Factory canteens	17	467
Camps	2	181
Hospitals	10	405
Local authority institutions	3	319
At home	132	1418
Other places	12	470
Unknown	60	444
	300	5966

The White Loaf

In reply to Dr STROSS Dr CHARLES HILL, parliamentary secretary to the Ministry of Food said that precise information as to the response of the public to the availability of the white loaf would not be available until the December claims for bread subsidy came in from the bakers. It appeared so far that while there were many local variations the total transfer of demand from National to whiter bread was small He had no doubt that the National loaf was the healthier loaf what had been done was to give the public freedom of choice

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[1] See *Lancet*, Aug 15 1953 p 347

Flour Improvers

Dr Stross asked the Minister of Food when the use of agene as a flour improver and bleacher would be discontinued, and what other substance would be used in its place — Dr Hill replied Although good progress has been made the investigations are not yet complete I hope, however, to be in a position to make a statement within the next three or four months

Milk-borne Diseases

Replying to Dr A D D Broughton, Dr Hill said that 48% of the population of England and Wales, and 63% of the population of Scotland, resided in areas specified by Orders which had been made, or which were now laid in draft, before Parliament for the purpose of protecting the public against milk borne diseases

Royal Commission's Terms of Reference

Replying to a question, Mr Macleod said that it would not be appropriate to extend the terms of reference of the Royal Commission on the laws relating to mental disorders to cover the law with regard to homosexual cases and their medical treatment In so far, however, as they might be suffering from mental illness or mental defect, their position as regards certification, detention, and care would be covered in the same way as that of other persons so suffering

Medical Services on Royal Yacht *Britannia*

Replying to a question, Mr J P L Thomas, First Lord of the Admiralty, said that 200 hospital beds could be accommodated in the royal yacht, the estimated cost of supplying and equipping these beds and ancillary medical services was approximately £12,000

Nurses' Pay in R.A F Tuberculosis Wards

Replying to a question, Mr George Ward, under-secretary of State for Air, said that an extra 3*s* a day was paid to nursing officers of Princess Mary's Royal Air Force Nursing Service below the rank of wing officer when employed full-time on nursing pulmonary tuberculosis cases Airmen on this work were given an extra 6*d* a day, and airwomen an extra 5*d*

Mr P F Remnant Does the Minister deny that there are any special risks in serving in these wards on account of the precautions taken ? Mr Ward There is no evidence that the incidence of tuberculosis among, for example, R A F ward orderlies is higher than the incidence in the R A F as a whole, and any extra risk is counteracted by the precautions taken.

Dr Edith Summerskill Is the Minister aware that the younger these individuals are the greater is their vulnerability to this disease ? Does he consider 5*d* sufficient compensation for the risk these girls take ? Mr Ward One test to which they are subjected before being allowed to undertake this work is the Mantoux test, which shows whether or not a person is liable to tuberculosis Mr A Woodburn Is the Minister aware that the health authorities do not regard it as desirable that it should be suggested that the nurses in this type of nursing are open to any greater risk than they are in an ordinary accident ward, where a proportion of the patients may be suffering from tuberculosis, just as in tuberculosis hospitals ? Mr Ward Yes, Sir As far as the R A F is concerned, our practice is in conformity with the practice in civil hospitals

Myxomatosis

In answer to a question, Sir Thomas Dugdale, Minister of Agriculture, said that all reasonable practicable steps were being taken to stamp out the only two known outbreaks of myxomatosis that had recently come to light in Kent Measures were also being examined for the protective inoculation of tame rabbits in case myxomatosis should spread Future policy would be determined in the light of recommendations from the advisory committee which he and the Secretary of State for Scotland had set up and which is holding its first meeting next week.

The chairman of the committee is Lord Carrington, and the members include Dr C H Andrewes, F.R S

In England Now

A Running Commentary by Peripatetic Correspondents

In Cuba now—or at any rate a short while ago—the pædiatricians assembled for their international congress had castanets for breakfast and music most of the time. Since parliamentary government is temporarily suspended, the beautiful National Capitol in Havana was available for the main events of inauguration and registration Conveniently across the road (crossed by keep-to-the-left motorists at great peril) was a air-conditioned cinema which housed the main [illegible] by day and Charlie Chaplin in what was obviously the Spanish equivalent of *Limelight* by night Projection was not always as good as might have been expected in a cinema, but the simultaneous walkie talkie translation apparatus was mostly a boon

Quite suddenly, so it seemed, it was decided one [illegible] to take all the congress (said by now to number up [illegible] 2000 with wives et al) thirty miles to see a n[illegible] orphanage-technical school for the children of [illegible] Coaches were to leave at 11 A M.—well, 12 noon—but then there was a mass photograph, so we embarked [illegible] 12 30 and about 12 50 we were installed all along [illegible] charming sea front where the north wind of early N[illegible] was blowing spray on to the road Finally all [illegible] assembled and off we went In front two motor-cycles carried the Cuban equivalent of "traffic cops" with screeching syrens followed by the President of the Congress Pot-holes added hazards to the early part of the journey, the principle being that it was stupid to repair them until the rains had really ended (? November). Yet marvellous new buildings had to be inspected on arrival while blood-sugars sank lower, and it was nearly 3 P.M. before we sat down to be waited upon in a vast dining-room by girl orphans who looked like a chorus from *Daddy-Long-Legs* or *Love from Judy* Round-table study groups had been scheduled for 2 P.M and many had been lured on the drive by the statement that they were to be held at the site of lunch, but this was cancelled so all except those who attended the "Grand Council" were whisked back to town again, screaming past red lights—the syrens, not the delegates—for a late start Unfortunately the "round table" included several members of the council and this group did not get going till next day, 27 hours and 20 minutes behind official schedule

The local rum cocktail gave great pharmacological interest to the proceedings One bar appeared to give these away at lunch-time, and many pædiatricians found they just could not compete with the bar-tender There was a touching sight of a tough Texan (probably) staring sorrowfully at a row of drinks on which he was fighting a losing battle At my hotel two drinks for the price of one encouraged the unwary to start at 5 P.M. One theory was that rum deadened the noise outside, which seemed unending, although a British pædiatrician awake at the uncomfortable hour of 4 A.M. asserted that it was quiet then The famous Morro Castle (about the same age as the Royal College of Physicians of London) contained a working life-size model of the garrotting machine, and at least one member of the inspecting party left hurriedly as a voluble guide demonstrated its use

* * *

I rush from my operating-list to the outpatients and then on to a ward round But one of the joys of "the end in sight" is to relax with the last few patients and hear something of their views on life and their ways of living My latest patient friend is a farmer and a cheese-maker who relaxed once too often in the presence of his bull "This penicillin," he says, "may be a wonderful thing for me in here, but it costs me thousands outside. Now and then, and it is becoming an increasingly frequent occurrence, we find that thousands of gallons of milk won't make cheese The 'starters' are not there, and it is all thanks to penicillin which is being used in the treatment of mastitis in cows" "What's the answer?" I ask him He shrugs his shoulder philosophically "At present none, but of course it isn't all waste. The milk is still fit for human consumption"

My tired mind goes back to the little boy I saw early in the day He had osteomyelitis presenting with [illegible] sions, one in his femur on the right side and the other his tibia on the left, and the organism has proved trangely confident in the presence of penicillin despite he assurance of his family doctor that as far as he knows he boy has never had penicillin I remember two other atients I have seen lately with multiple lesions and the ittle girl with the pyogenic abscess so chronic that it ppeared almost a tumour Perhaps the milk that has o "starters but is fit for human consumption fits into he jigsaw somewhere No matter with what benevolent ntentions we interfere with the balance of Nature we o it at a peril

* * *

Our tame psychiatrist refused the offer of a couple of oose eggs, but his small boy was persuaded by the ardener to put them under his bantams The cock and is three hens got straight down to the job, never less than wo of them sitting at any given time on the eggs till hey were hatched The cock, who took his fair share of he work of brooding, now proudly leads his wives and he two goslings round the garden. Surely an ornitho-ogical event of the first importance, and perhaps unique?

* * *

The placebo has been receiving a lot of attention lately, ut no-one has mentioned what I call ' placebo diag osis '—the common everyday terms we use in a busy urgery Two popular ones are

Teething—I may explain to a mother that her fretful child ho is not really ill is teething The mother who really knew his all along, goes away happily and no doubt gets on with he child better now she is sure what ails it I know that no-one nows what *symptoms (if any) teething causes* *Some paedia-*ricians say it can cause none while others say it does cause yrexial illnesses that fall by crisis as a tooth appears. I had o trouble with my wisdom teeth, but I know doctors who o, and they firmly believe in painful teething I just don t now who is right but I go on using teething as a diagnosis. t satisfies the mother and when used wisely is harmless. No oubt it is sometimes correct

The Change.—This is one I do not like for what psychological eason I do not know Again no-one knows what if any ymptoms are caused by gonadal old age If the symptoms o, not indicate disease we may perhaps accept the patient s iagnosis (though I never proffer this one myself) Œstrogens o help sometimes, though whether a placebo would I do not now

Every doctor has his favourite diagnosis that in truth s not reasonable—catarrh, the monthlies, rheumatism, onstipation low blood pressure high blood pressure, erves, obesity, and dropped viscera. Psychoneurosis nd teething I use others still favour constipation or grumbling appendix. Yet others go straight for landular *fever or brucellosis. But why, oh why does the* atient seem quite content with the thought that he has gastric stomach or a cardiac heart?

* * *

We were gently tossing in Charlie s 16-ft. motor-boat, hiffling up and down the bay for mackerel and pollack. t was a grey day at sunset, just the day to catch fish Ve were using the new fangled snare of 16 feathered ooks, with which we had done so well only the other vening We were off the approved mark—Tonkin s ellar Row—where last year we caught 3 four pound ollack at one pull, and Roy had that fine sea bass. espite all these propitious occurrences we had no bite or the evening Charlie s normally cheerful face was lum I reckon tis more comfortable at home Ted —unheard of sentiments from Charlie at sea. Then we aw an old whiskered face lift from the seas about a undred yards from us. It was the seal that sometimes ooks on Holzephron or Parc Vean beach, out fishing for is supper

Ah, says Charlie, That ole seal s driven the fish way We ll go down along a bit. Sure enough, hen we got down off Gwinian Point there were pollack hick and fast, and we had good sport. Now what want to know is, if the seal has this effect on the fish n his neighbourhood how does he make his living fishing?

* * *

"Has the House Surgeon examined this patient Nurse?"
"Yes r he did a digitalis examination"
"Ah! with a foxglove I presume"

Letters to the Editor

VAGARIES OF INTELLIGENCE

SIR,—The pronouncements on the constancy of the I Q in your issue of Oct 24 have been widely quoted in the press, and I should therefore be grateful if I might remove one or two misconceptions

The criticisms of the I Q brought forward by the three young investigators whom you mainly quote are by no means as new as they suppose Dr and Mrs. Clarke declare that the fact of I Q variability can no longer be disputed. ' But who has ever disputed it? In criticising previous views they refer, among other publications, to an L C C report of my own and add these investigators rarely if ever submit their hypotheses to experimental proof. ' The report was first published, not in 1947, but in 1921 Results were then given for cases retested annually for 5 years, and I emphasised that the constancy of I.Q ' is but imperfectly realised. ' In later reports data were given for cases followed up for 25 or 30 years The experimental proof " of Dr and Mrs. Clarke covers an average period of 2 years 3 months only

In an earlier report (1917) I insisted that ' for scientific work the employment of the standard deviation (or its equivalent—the percentile) seems indisputably the best device," and merely proposed a quotient or ratio because it could be rapidly calculated and seemed more intelligible to magistrates and medical officers. The quotient,' it was explained, assumes as a first approximation that the changes in mean mental age and in the standard deviation are rectilinear, whereas in fact they are curvilinear " This simplification is the main (but not the only) cause of the inconstancy Your contributors seem to be wholly unaware that psychologists, not only demonstrated the existence and amount of error to be expected but showed how it could largely be corrected by adopting a more complex formula This entails a *statistical analysis of a rather elaborate type* the most recent suggestions will be found in an article by Dr Fraser Roberts,[1] based on tests applied at Stoke Park Colony and the Royal Eastern Counties Institution Every psychologist will therefore welcome what you say in your leader on the need for publicising the value of statistical research.'

One important cause of variation is not mentioned by your contributors—the fact that so many of those who employ (and criticise) intelligence tests have never been trained in their administration and interpretation. Dr Tizard states that an I Q of less than 70 is very widely accepted as evidence of mental subnormality sometimes on the basis of a single test Presumably he is referring to the standard proposed for certifying special-school cases in the days when such cases had to be certified Possibly some medical officers have relied on a single test But no trained psychologist relies on tests alone—much less on a single test—in any doubtful case

In your leading article you seem to confuse three different concepts that psychologists have carefully distinguished first, the innate general cognitive factor (γ), secondly the estimates obtained for such factor measurements (*g*); thirdly the vague qualities called intelligence ' in everyday speech To prove that the last can be altered by education or that the second provides only rough and fallible assessments is not to demonstrate that the first—an entirely abstract and hypothetical component—is subject to variability The psychologist, like the physicist, has adopted a popular word to avoid pedantic symbols and circumlocutions but, in criticising what he says about intelligence ' as he has defined it, arguments based on some other interpretation seem (if I may say so) merely to confuse the issue

University College
London, W C.1

CYRIL BURT

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1 Roberts, J A. F *Brit J statist. Psychol* 1952 5 65

MILLI-EQUIVALENTS

SIR,—In articles, often by clinicians, I note the liberty with which certain blood components are expressed in milli equivalents, yet other acid and basic radicals are referred to in a different value—e g , grammes per 100 ml or even as a " normality " Thereby the usefulness of the m eq expression as a convenient index in acid/base balance studies is lost , presumably the author only intends to convey the blood concentration of an element The actual estimates of such substances (K, Na, Cl, &c) by a laboratory are in terms of mg per 100 ml , and—which is more important—replacement is by a grammes per litre solution

In a recent authoritative paper a prescription for replacement therapy in cases of ileus is expressed in terms of both presentages and milli-equivalents Surely, Sir, this makes for confusion and opens the door to serious dispensing errors

True, by using a simple formula one method of expression is easily convertible to another, but for practical purposes it is surely more useful to retain mg per 100 ml —the form in which, I believe, most clinicians think, and of which they know the normal blood-levels

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J E ENNIS

HYALINE MEMBRANE IN THE NEONATAL LUNG

SIR,—We must be grateful to your contributors who have recently established " hyaline membrane " in the lungs of the newborn as an important disease entity at long last It is evident, however, that some issues, which probably could be solved, are still confused

Dr Emery (Oct 24) must be correct in deprecating the application of either positive or negative findings in animal experiments to the human problem The animal fœtus differs from the human in various ways, notably the lack of a comparable coating of vernix caseosa, and the absence of anæsthesia in the mother The only satisfactory starting point for experiments cannot be obtained—i e , the human fœtus before it takes its first breath I believe there are enough experiments unwittingly performed at cæsarean section to enable us to forget experimental animals—especially those in which the animals have been breathing air for quite a long time

I do not share Dr Emery's view that the hyaline membrane of the newborn is comparable with membranes developing later in life—e g , in nephritis, rheumatic fever, and cardiac failure The nearest approach I have seen was in a patient with extensive amyloid disease It is this general (and I think erroneous) belief which has led to the disuse of the name " vernix membrane " While I do not suggest that " vernix membrane " is more than a part truth, it is a romantic name and the one I prefer To me at least, " hyaline membrane " not only contains no truth at all but leads us along wrong lines in research The Oxford dictionary states that " hyaline " means glassy The membrane in question is seen in routine sections (hæmatoxylin and eosin) to be an opaque dirty red—not my idea of glassy Because the name given to this membrane appears capable of arousing deep feelings I have suggested that we call it " alveolar-duct membrane," after its distribution There appears to be general agreement on two points only—that it occurs in alveolar ducts and that it does not occur in stillborn infants

There are three possible lines of inquiry, of which only the first lies predominantly with the pathologist

(1) What substances unquestionably enter the bronchial tree in stillbirths? Here it is necessary to point out that, with few exceptions, " sudden death " does not occur at any stage of our intra or extra-uterine life The commonest " sudden death " is coronary thrombosis, but this is not really sudden in the sense that everything stops just as it was I have, for example, never heard of an accident resulting from the " sudden death " of a car driver Likewise, the fœtus dying in utero does not just stop suddenly at a particular point in its development Whatever the cause, an asphyxial state develops This leads to the inhalation, firstly, of the substances already in the mouth and pharynx, such as mucus and nucleated epithelial squames, and, secondly, of liquor amnii with its suspended vernix caseosa, epithelial squames, meconium, &c

The amount of vernix entering the lungs is very variable, as might be expected from the variation in the amount seen on newborn babies It may enter the lungs in two ways: firstly, as amorphous masses of vernix itself (I recently examined the lungs of a stillborn infant in which there were great masses of it in the alveolar ducts and alveoli, but this is exceptional) , secondly, anyone who will examine a fat stain of skin from the groin and elsewhere will see that the epithelial squames are heavily coated with vernix, and that these squames are cornified and do not have a nucleus. I find it difficult to assess histologically the proportion of nucleated to cornified squames in the bronchial tree and alveoli, but my impression is that the former (of oropharyngeal origin) predominate Some obstetricians insist that these oropharyngeal substances are very important in the production of alveolar duct membrane Mr L O Watt evolved a technique for removing them from the upper air passages of the newborn (especially after cæsarean section) and he believes this produced a much higher proportion of healthy babies

Pathologists and pædiatricians must carefully findings of the obstetricians, for I feel sure that it will be the clues supplied by the obstetricians which will finally solve the problem

Originally, we thought the " vernix membrane " was entirely due to inhaled substances, now it is quite " low-brow " to think these have anything to do with it at all Surely the pendulum has swung too far To me alveolar-duct membrane has a complex and variable composition, it includes mucins, fats, epithelial squames and possibly unknown elements from the alveolar ducts and blood-stream Blood elements do not appear to be essential because there may be a thick membrane with no œdema at all, and there may be gross œdema with or without membrane

Dr C G Paine is probably correct in stating that the fat content of the membrane decreases with the age of the baby This may not be a fundamental observation because macrophages appear to attack fat before anything else. Vast numbers of squames may be inhaled without any membrane forming, and many membranes do not appear to contain squames It is difficult to believe that the squames are an essential element of the membrane, partly because they enter alveoli so readily, unlike the alveolar duct membrane

It is interesting to see that Dr Claireaux (Oct. 10) finds many nucleated squames in the deposit from the liquor amnii It is possible that these are contaminants from the maternal cervix and vagina, and that the fœtus could also inhale them before the membranes rupture or until the head is in the vagina It is difficult to tell vaginal squames from those formed in the oropharynx of the fœtus, they will not come from the fœtal skin Whatever their origin, there is no doubt that nucleated squames do gain access to the fœtal air-passages and often, I think, outnumber cornified squames with no nucleus

(2) I think it probable that the best line of inquiry is open to the obstetricians alone In my early work on alveolar-duct membrane, I was surprised to find that it was a common cause of death in babies delivered by cæsarean section. The must eliminate vaginal nucleated squames as the cause of alveolar duct membrane Some years before he retired from the staff of the Derbyshire Hospital for Women, Mr C G Lochrane was much concerned by the number of babies who died of this condition after cæsarean section. He discussed this with Mr R J M Jamieson (now his successor and they concluded that the probable cause was the failure to deliver the baby before it had become appreciably anæsthetised or cyanosed Mr Jamieson was given the task of administering this type of anæsthetic and the deaths ceased

Possible confirmation of this belief comes from Dr Pa who tells me that, of many cæsarean sections performed under local anæsthesia at the Jessop Hospital for Women, Sheffield, none has produced a baby who has died from alveolar duct membrane If this is so, then surely it is a vital observation in explaining the cause of the membrane.

(3) The third profitable inquiry is indicated in the article by Mr Donald and Dr Steiner (Oct 24)—an outstanding

valuable study I think that in time they will prove that alveolar-duct membrane is not always fatal In the past, radiologists have made a definite diagnosis of bronchopneumonia on the findings they describe In some of these I have found a normal blood picture and observed a normal temperature chart I have therefore concluded that they were cases of alveolar duct membrane which recovered though final proof was of course lacking

I doubt if Dr Steiner is wise to complicate the subject by including post-mortem pictures. Many of these will show oedema and not collapse The word 'collapse must be used with care because most of these lungs are not greatly reduced in volume The reason for this is that the respiratory forces lead to much ballooning of the alveolar ducts when the alveoli can no longer expand and contract normally—an appearance often erroneously called emphysema

I hope the work at Hammersmith will be continued indefinitely so that it will be possible to obtain a very long follow up in those cases of probable membrane which recover It is at least possible that the ballooning of the alveolar ducts which occurs when a membrane is present will be followed by bronchiectasis in later life

It is my belief that alveolar-duct (or hyaline) membrane is a lesion which is secondary to preventable causes It is more than probable that if the obstetricians pooled their knowledge and experience we would soon know instead of guess these causes

Derbyshire Royal Infirmary
Derby
G R OSBORN

RESETTLEMENT OF DISABLED PERSONS

SIR,—Nobody in the medical profession has done more for the cause of rehabilitation and resettlement of the disabled than Sir Reginald Watson-Jones—as I know from personal experience

When a representative of the Ministry of Labour states that we in this country are away ahead in the solution of this difficult problem I think he has been allowed more than his quota of poetic licence Ahead in social legislation perhaps but in the general application of the principles of rehabilitation we can learn from other countries.

I have recently been the deputy director of the United Nations course on Rehabilitation of the Adult Disabled held in Sweden Finland, and Denmark Some Scandinavian countries can teach us the integration and coöperation of government services, the medical profession, and the voluntary agencies. It is this very integration that is missing in this country The unemployed disabled person is influenced by the Ministry of Health organisation whilst under medical control by the Ministry of Labour when he seeks employment and re-training; by the Ministry of Pensions and National Insurance when he requires an invalid carriage or when his sickness benefit is not forthcoming by the National Assistance Board when he requires extra help by the Ministry of Education if he is an adolescent and needs further education The various representatives of these official bodies give him conflicting advice In addition, he is also influenced by trade union representatives, lawyers, and well meaning friends and relatives He is also guided by the various voluntary agencies whose aims are to help the disabled Can it be wondered at that during the period of his rehabilitation he is confused anxious, and in the end frustrated

Rehabilitation, in my opinion is a medical problem, because without good health we cannot have good industry Resettlement is partly medical and partly the province of the Ministry of Labour Re-training must be controlled by the Ministry of Labour

Is it possible for us to remove the patient from the realms of "power politics ' and institute one authority empowered to guide the patient into the safe harbour of gainful employment? I believe if we spent less time in apportioning blame and gave more thought to what is happening to the patient s morale we should be rewarded by seeing disabled patients living and working happily—restored to life in its widest sense That is our aim

Garston Manor Rehabilitation Centre,
nr Watford, Herts.
C J S O'MALLEY
Medical director

CHILDREN IN HOSPITAL

SIR,—As one who has over the last thirty years been associated with work in children s hospitals, particularly orthopædic hospitals, I should like to endorse the views expressed by Dr Mac Keith (Oct. 24) concerning children who require operative treatment.

Any attempt to bluff or deceive children is doomed to failure as they seem to possess a sixth sense by which they easily detect such efforts Nevertheless, operations and particularly orthopædic operations can be very painful unless the proper preoperative and postoperative treatment is given and I write to make a plea for the proper postoperative use of morphine for children

It seems that in some quarters there has arisen a tendency to teach that morphine is dangerous for children but I should like to record that after using it for thirty years according to the formula of age over age + 12 I have never had any anxiety Not only is it not dangerous but children in pain seem to thrive on it After an operation, such as arthrodesis of the hip the child who has had proper doses of morphine is found next day to have a good colour and to be comfortable but when meagre doses of 'Nepenthe have been given the child is pale and miserable

With the proper use of morphine it is possible to assure a child unreservedly that he will not suffer much pain; and the child awaiting operation will have observed that his next-door neighbour who has already had his operation had quite a comfortable time of it Under these conditions children fear operation much less.

Black Notley Hospital
Braintree Essex.
M. C WILKINSON

SIR—All who work with children will be grateful to Dr Mac Keith for his article One small criticism I would like to make is against the suggestion that, in preparing the child for entry to hospital for an operation he should be given a mental picture of the operating theatre and white-gowned nurses. Surely this is unnecessary since no child should be allowed entry into the operating theatre while still conscious?

South Devon and East Cornwall Hospital
Plymouth.
HUGH JOLLY

INTRA ARTERIAL TRANSFUSION

SIR,—Dr Brown's article (Oct. 10) on intra-arterial blood transfusion after controlled bleeding emphasises the advantage of the arterial over the venous route for transfusion in cases with prolonged hypotension and peripheral vasoconstriction after hæmorrhage.

While the radial artery is suitable for transfusion in cases such as his where the cannula can be tied in before vasoconstriction develops, the position is otherwise when the limbs are cold and exhibit severe vasoconstriction In such cases difficulty in inserting a cannula in the radial artery and in securing an adequate inflow of blood has been reported[1] Probably the chances of gangrene in the hand are enhanced in these circumstances, and the risk of this and other complications is by no means negligible. Thrombosis of the femoral artery has followed its use for transfusion,[2] so this route is not to be recommended

Dr Brown suggests use of the aorta as a last resort, but my experience indicates that no complications or difficulties attend intra aortic transfusion when my special needle is used[3] and therefore this should be the route of choice

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[1] Porter M R., Sanders L. K., Lockwood, J S *Ann Surg* 1948 128, 865

[2] Lleras, Vicuna and Leca. *Afr franç chir* 1949 p 237

[3] Haxton H A *Lancet* 1953 i, 622.

The evidence from animal experiments and clinical trial is now overwhelmingly in support of intra-arterial transfusion as the only measure which will save life in cases where shock from hæmorrhage is of sufficient severity and duration It is sad, therefore, to think of the many lives lost every year which could probably have been saved by this measure It is surely not too much to hope that soon every hospital of any importance will have the equipment for intra arterial transfusions and staff who are prepared to use it

Crumpsall Hospital,
Manchester

HERBERT HAXTON

TATTOOS

SIR,—I have read with great interest your annotation last week on this subject However, it surprises me that you do not accord to viral hepatitis a place in the list of potential complications of deliberate tattooing carried out for purposes of adornment

Hobson et al[1] investigated this question among patients in a military hospital in Hong-Kong—a group among whom tattooing was popular and viral hepatitis prevalent They found that, out of 143 patients admitted with viral hepatitis during a certain period, no fewer than 56 (or 39 2%) had been tattooed between 51 and 150 days prior to the onset of the disease As controls, they took 152 patients admitted during the same period for other complaints In this group the number tattooed during the corresponding period was only 16 (10 5%)

They also describe the modus operandi of a local tattooist, their description lending eloquent support to the belief that the virus may be transmitted in this way

Department of Pathology,
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London, S E 1

G A K MISSEN

TUBERCULOSIS

SIR,—May I answer the letters of Dr Paul and Dr Hoffstaedt (Oct 10)? Perhaps our differences are not o great as they appear, although it is necessary to correct npressions that may have been given concerning the control of tuberculosis in cattle It is true that bovine tuberculosis was virtually eradicated in the U S A 23 years after the inception of a nation-wide campaign in 1917, but at that time the over all incidence in adult cattle was only about 4%, compared with about 25% in Great Britain in 1935 Again, 16 years ago in Denmark 48 5% of all herds had been tuberculin tested and 26% of these were free from infection In Great Britain there was no effective scheme for the control of bovine tuberculosis until 1935, and owing to a Government decision no new attested herds were created during the war In 1944 there were only some 600,000 cattle in these herds By 1946 the number had increased to 1 million (about 13% of all cattle—i e, roughly comparable with the Danish picture in 1937) and by 1952 to 3½ million There are now some 4 million cattle in attested herds out of a total of about 9 million, so at the present rate of progress tuberculosis should be virtually eradicated in 10 or 12 rather than 34 years

To suggest that injection of the B C G strain of avirulent tubercle bacilli increases the incidence of bacilli in the population is rather like saying that vaccination increases the incidence of smallpox virus—although one admits that even this procedure has its opponents

Dr Paul still seems very unconcerned about the presence of virulent tubercle bacilli, and Dr Hoffstaedt even suggests that it would be unfortunate if we attempted to "banish from our shores a virtually ubiquitous and mostly quite harmless germ" "Mostly quite harmless" seems a strange description to apply to an organism that, as Rich says in the last sentence of his book on *The Pathogenesis of Tuberculosis*, still kills more than twice as many people as any other single cause of death during the particularly productive and enjoyable period between the ages of 15 and 45 He points out that increased genetic resistance cannot possibly be the sole reason for the precipitous fall in the mortality rate that occurred within a scant two generations Even if it were entirely responsible, Sir Macfarlane Burnet[1] has indicated that it would take centuries before resistance fell to that of, say, the American Indian

The elimination of most infectious disease doubtless tends to increase the susceptibility of the population, but few people think it desirable that we should continue to have a good infection-rate with such organisms as *Corynebacterium diphtheriæ* or *Treponema pallidum* If it were desirable to maintain tubercle bacilli in the population there would, of course, be no reason at all for public health doctors to worry about tubercle bacilli in milk, for, if one must be infected, the alimentary route is much less dangerous than the respiratory Mr L Pitcher has devoted much energy to attempting to show that as one eradicates tuberculosis from cattle the death-rate from pulmonary tuberculosis increases It is probably true that under certain conditions, which may have prevailed in Great Britain, tubercle bacilli in milk decrease the total death-rate from human tuberculosis, but Dr Daw[3] rightly questions Mr Pitcher's argument and asks for more evidence One may say briefly that the mortality from human tuberculosis has continued to fall steadily in the U S A since the virtual eradication of bovine tuberculosis This is also true in Tasmania and in Queensland (an area mentioned by Mr Pitcher as having a low human mortality and at one time high incidence of bovine infection) Above all, both human and bovine infection have been eradicated from the island of Bornholm

I agree of course with Dr Paul and Dr Hoffstaedt that a general improvement in living standards is probably the most important factor in reducing the mortality from tuberculosis Various predictions that tuberculosis would become extinct by a certain date through the operation of such natural causes have however been falsified, and it is salutary to remember that only 53 years after syphilis appeared in Europe Fracastorius wrote "Whatever may be the cause we must conclude that this disease has now entered its old age, and that the time is not far off when it will cease to propagate itself" As one would expect, the best results in the control of tuberculosis have been achieved when specific attempts to prevent the spread of tubercle bacilli have been combined with good living conditions, and the mortality rate is now below 10 per 100,000 in Denmark and in certain States in the U S A, and is only 11 per 100,000 in Tasmania

Dr Paul suggests that I am confusing the eradication of tuberculosis with the eradication of the tubercle bacillus In an essay on the Natural History of Tuberculosis Sir Macfarlane Burnet[1] wrote "To prevent disability and death from tuberculosis the one outstanding requirement is to prevent primary infection with the bacillus" Or, as Sir John M'Fadyean wrote in 1901, "all efforts must be concentrated against the one great cause of the disease—the operation of contagion" Myers has said much the same thing on many occasions, but it would seem that the truth of these statements cannot be too often emphasised Sir Macfarlane's essay no doubt influenced the scheme for the control of tuberculosis in Tasmania, and if he reads it Dr Paul may discover some alternatives to the method of slaughter Incidentally we have eradicated tuberculosis from 40% of our herds without slaughtering, for this purpose,

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[1] Hobson A C S Fraser D E Newman N H *Brit med J* 1952 i, 1111

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[1] Burnet F M The Background of Infectious Diseases in Man Melbourne 1946
[2] Francis J *Lancet* 1950 i, 34
[3] Daw R H *Ibid* 1952 ii 1272

single unoffending cow, although our failure to do so has annoyed a good many people

When in 1895 the use of tuberculin had revealed the high incidence of bovine tuberculosis in Great Britain it was concluded that any attempt at eradication was quite impracticable It was true that sudden radical measures were impracticable and nothing was done for some 40 years during which time the incidence of infection remained nearly constant but as soon as the community decided it would try to eradicate the bovine tubercle bacillus it was found that steady progress could be made, and eradication areas have now been established I realise that eradication of human infection is a far more difficult and complex task, but let us agree that the presence of virulent tubercle bacilli in the human population is as undesirable as it is in cattle It may then be found sooner than some people expect, that improved living conditions allied with specific measures against the tubercle bacillus, which I am sure would have the support of Dr Paul and Dr Hoffstaedt, have reduced the incidence of infection to such a low level that virtual eradication is not an impossibility It is a matter of fact that good progress towards eradication of the tubercle bacillus has been achieved in several communities without apparently exciting any serious opposition

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JOHN FRANCIS

CONTROLS

SIR —It is a matter for regret that the use of normal children (or children suffering from some irrelevant disease) as controls in clinical research appears to be increasing

No medical procedure involving the slightest risk or accompanied by the slightest physical or mental pain may be inflicted on a child for experimental purposes unless there is a reasonable chance, or at least a hope that the child may benefit thereby

If this is true—and I hope that there are few doctors in this country who would disagree—then it must surely be difficult to justify the use of two hydrocephalic infants reported in the paper by Dr Doxiadis and his colleagues, and the use of a normal control by Dr Bickel and his colleagues Both papers appeared in your issue of Oct. 17

It may be of course, that there were some good reasons for the use of these children which have not been made clear If so, the authors owe it to themselves to explain

London, N 1

R E W FISHER

*** Dr Doxiadis is now abroad, but we have shown the above letter to the other medical authors of the two papers. They reply as follows

'It is quite reasonable that Dr Fisher should raise the question of the use of normal children or children suffering from some irrelevant disease as controls in clinical research There are extreme opinions on both sides, but I feel most of us adopt a policy between the two—somewhere in the grey between the rather theoretical white and black My own working policy which differs slightly from that expounded by Dr Fisher in the second paragraph of his letter is that no procedure should be carried out involving risk or discomfort without a reasonable chance of benefit to that child *or other children* and this principle was followed throughout our work. The crux of the matter is contained in the last sentence of Dr Fisher s letter—we owe it to ourselves to explain our actions Surely we all weigh these matters most carefully in our own consciences. —K S. HOLT

We are grateful to Dr Fisher for raising a problem of which we are fully conscious in our daily work Nevertheless errors of metabolism constituting the underlying cause of many diseases cannot be understood or properly treated without knowledge of normal physiology With regard to our own work phenylalanine is an essential article of the diet, and Rose [1] recommends a daily intake of 2 2 g Earlier work on normal adults [2,3] and on children [4,5] has shown that considerably larger amounts of phenylalanine may be ingested, as they are rapidly metabolised and cause no untoward effects. Our work was undertaken to observe the blood levels of a normal child after doubling the normal phenylalanine intake in order to compare the normal tolerance curve with the pathological curve in phenylketonuria. This may be regarded as closely comparable with a glucose-tolerance test in that it is both harmless to the normal and of great importance for the assessment of pathological curves ' —H. BICKEL, J GERRARD

BASIC GROUP PRACTICE

SIR —We have followed, with great interest, the series of articles on general practice which have appeared from time to time in *The Lancet* under the name of Joseph S Collings We have been impressed with the tireless energy he has displayed in pirouetting round this country studying and reporting on individual practices and issuing reports on how general practice *really* ought to be conducted. Then we read in his article of Oct. 24

> In its first five years the National Health Service has done little to stimulate the development of group practice Hopes were centred at first on the possibilities of ill-defined and little understood health centres ; but these hopes have only been fulfilled in two or three places and by now have lost their charm both for the general practitioner and for the Exchequer They are monuments to the local authorities and the outcome of a do nothing policy in regard to the main structure of general practice '

Such ex-cathedra statements are rather mischievous particularly when we know that Dr Collings has never taken the trouble to visit the William Budd Health Centre in Bristol to find out what progress has been made

If he is so ready to condemn health centres which as yet have had little chance of proving themselves, and even without any first-hand knowledge of how at least one of them is working then we fear we must reconsider our judgment of the value of his previous articles

Bristol.

R C WOFINDEN
J SLUGLETT

PERIODIC MEDICAL OVERHAUL

SIR,—Sir Adolphe Abrahams generalises against periodic overhauls on the basis of three cases, although undoubtedly he could cite more Surely no-one in medicine, least of all Sir Adolphe with his vast experience, would suggest that any examination, advice or treatment was likely to be 100% successful in all cases.

What does Sir Adolphe mean by sensible people ? As regards health few people are sensible. Has he never met any people, even doctors who have had headaches, indigestion piles, or a cough for months and who have never done anything about it and eventually been found to be severe hyperpietics or to have inoperable carcinoma or advanced pulmonary tuberculosis ? Admittedly many of these people would not have a periodic overhaul anyway but the whole idea of such a check is to try and catch *some* of the early cases of tuberculosis, carcinoma, anæmia hyperpiesia, diabetes, &c explain what is wrong and help them to be relieved or cured before they become invalids

There are difficulties in that few even intelligent, people will give the time to have an overhaul or they are scared of the possible result and the doctors in the National Health Service have not got the time or the facilities to do their job as they would wish

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1 Rose W C. *Fed. Proc* 1949 8 546
2 Penrose, L., Quastel, J H *Biochem. J* 1937 31 266
3. Jervis, G A. *J biol Chem.* 1947, 169 651
4 Woolf L. I., Edmunds, M. E. *Biochem. J* 1950 47 630
5 Levine S Z. Dann M., Marples E. *J clin. Invest.* 1943 22 551

Those of us who have the time to take a proper history, carry out a detailed examination of the patient, and talk to him afterwards, know that hardly a day passes when someone is not found with some complaint which can be cured or at any rate ameliorated in its early stages and thereby save him a great deal of discomfort and possible anxiety in the future

Finally, if not the doctor, who would Sir Adolphe suggest is the best person to give common-sense health education ?

Hook, Hampshire R H SCOTT

POSTURE, BACKACHE, AND HEALTH

SIR,—In his letter of Oct 17, Mr Tucker describes an ideal posture and guarantees that if one learns to stand in this way *continuously* one never seems to grow tired Many different postures have, in the past, been advocated as ideals and their theoretical mechanical advantages have been described, but, as far as I am aware, little practical evidence has ever been produced to show that any of them have, per se, any influence on the incidence of postural disorders of the supporting tissues

Posture is the sum of the conditions pertaining at all the joints of the body In the majority of those postures which are regarded as bad, poor, or abnormal, no joint is outside its normal range of movement The crux of the matter therefore seems to be, why joint positions which can be utilised with impunity in some circumstances become fraught with danger to the joint tissues if utilised in standing

Joint tissues, although they are living tissues, conform, in their reactions to stress to the same physical laws as inanimate objects such as steel or rubber All the tissues which may be involved in maintaining the position of a joint —namely, bone, cartilage, muscle, ligament, and fascia— all these tissues are elastic to momentary stresses of a magnitude less than the breaking load each is deformed when stress is applied to it and recovers its original dimensions when the stress is removed On the other hand, these tissues react in a different way to *prolonged* stress A stress which is less than the breaking load will, if it is allowed to persist for longer than an optimum time produce a gradual progressive distortion of the tissues Moreover, part of this distortion will be permanent unless it is slowly corrected by a vital reaction within the tissues

In standing, the stress on any joint tissue is never as great as the breaking load, and it is therefore only the duration of the stress and not the stress itself—only the duration of the posture rather than the posture itself—which can cause permanent changes in the joint tissues In other words a posture which is maintained continuously for a long time will damage the supporting tissues irrespective of whether it is regarded as an ideal posture or a bad posture, whereas any posture into which the body can be painlessly moulded will be harmless if it is of a short duration

The work of Ingelmark and his colleagues[1] has suggested that the time factor may also be important in another way They have produced considerable evidence in support of the hypothesis that the nutrition of articular cartilage and the production of synovial fluid are, in part at least, dependent on the rhythmical compression and release of articular cartilage A corollary to this hypothesis is that continuous compression of articular cartilage by the continuous maintenance of any posture would adversely affect both these functions

Observation of people in the street or of any person who is unaware that he is being watched shows that natural standing (in contrast to that of a soldier standing at attention) is never a continuously immobile act A person stands still for a short time, then shifts his lower limbs pelvis, and trunk before becoming still again for another short period, and this alternation between movement and immobility continues throughout the stance The average duration of the immobile periods is only about thirty seconds.[2] Moreover, not only is the continuity of the stress on joint tissues repeatedly broken in this way, but different postures may be assumed during successive immobile periods, so that the tissues on the right and left sides of the body are alternately subjected to the greater part of the total stress

Because the method of normal standing is so much in keeping with the physical properties and physiological processes of joint tissues, it seems reasonable to suggest that aberrations of the normal periodicity of standing might have a closer causal relation to postural disorders than the form of the various postures which are adopted during that act It was observed in the course of the investigations quoted above that in a small proportion of the subjects studied each immobile period of standing was prolonged beyond one minute I feel it would be of interest if the incidence of such habitual prolongation of the immobile periods of standing could be correlated with the incidence of postural disorders

Anatomy Department,
University of St. Andrews. J W SMITH

COARCTATION OF THE AORTA

SIR,—We have read with great interest your excellent editorial (Oct 24) on this subject, and there is one point upon which we should like to comment

You say that direct aortography should always be used in the preoperative investigation of coarctation. This investigation, although undoubtedly more precise and informative than venous angiocardiography, is not without risk, principally because of the high concentration of dye which enters the cerebral vessels and the coronary arteries In addition, the retrograde route involves the use of a peripheral artery, and intubation of the main artery to one upper limb, with the risk (admittedly small) of subsequent arterial thrombosis and ischæmia of the limb Positioning of the catheter in the arch of the aorta is not as easy as it may sound, and in short the investigation is usually far more time-consuming, difficult, and hazardous than angiocardiography by the venous route.

In our experience, venous angiocardiography gives an adequate picture of the site and extent of the coarctation, of the aorta above and below, of the origin of the left subclavian artery, and of the collateral circulation in the majority of cases[1] The risk is very small indeed but sufficient contrast medium must be used (1-1 5 ml of 70% diodone per kg body-weight) in order to obtain a good result We believe that aortography should only be performed in cases in which venous angiocardiography has been inadequate, or in which special problems of diagnosis exist, or when the surgeon expressly requests it

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Hospital

J F. GOODWIN
R E STEINER

SIR,—You say in your leading article (Oct 24) that no entirely satisfactory explanation has been found for the dilatation of the vessel so often noted distal to the constriction You mention the defective structure of the aortic wall as a factor, but perhaps the most important cause of dilatation of this segment is the turbulence which must invariably be created there. While, from above, we have the blood passing through the narrowed part of the aorta under high pressure, below the constriction we find, as a result of the collateral circulation, a retrograde flow from the intercostal vessels into the distal segment, again at a pressure only slightly lower than that in the proximal part of the aorta Even when the coarctation is complete, as it rarely is, the blood-flow from the intercostals into the aorta must create a considerable amount of turbulence, and it would be surprising if some dilatation did not result The position ght perhaps be compared to the post stenotic dilata n associated with aortic or pulmonary stenosis, again bably the result of turbulence created in these vessels the blood flow through the narrowed orifice

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[1] Ingelmark R. E Ekholm R. *Uppsala LäkFören Förh.* 1948 53 61 Ingelmark R. E *Acta orthoped scand.* 1950, 17 303

[2] Smith, J W *Acta orthopæd scand* 1953 (in the press)

[1] Goodwin J F Steiner R. E Mounsey J P D, Mac A. G, Wayne, E J *Brit. J Radiol.* 1953, 26, 161

The late systolic murmur usually heard in coarctation the aorta is often attributed to increased blood flow ough the collateral channels, and to kinking of these sels. The murmur cannot be due to the blood passing ough the constricted part for obstruction may be nplete at this point That turbulence in the distal ment of the aorta plays a part in the production of murmur seems likely and it may indeed be the rce of this characteristic physical sign

ublin. **Risteárd Mulcahy**

THE FACE IN DIAGNOSIS

IR,—Mr StKatsareas's article last week (p 920) ntions an astonishing number of facial signs, but enture to suggest that two or three more conditions causes of conditions, might be included.

diagnosis of argyria of the face has sometimes n discounted because no possible cause for the deposit ilver could be found

remember an instance in question: a young woman her doctor were unaware of any possible cause for the mentation (a biopsy of the skin had not been made) l the patient produced an old prescription from another tor who had ordered pills containing silver nitrate for "indigestion. So successful were the pills that the lent continued to take them whenever she had indigestion her similar cases have probably occurred from time to time case was shown at one of the annual meetings of the ish Association of Dermatology in which there was con rable facial pigmentation of the argyria type but no sible cause could be found My attention had recently n directed to the occasional occurrence of facial argyria to the use of a lotion containing Argyrol for the treat- nt of sore throat The general public was not aware hat time at any rate, that argyrol was a silver preparation questioning the patient admitted that he had been using outh wash or gargle for the throat. His doctor wrote he a few days later to say that on going further into the he had found that the patient had used a prescription taining silver nitrate

number of other conditions might be included

here is a possibility of pigmentation of the face being ed by the internal use not of silver but of bismuth.[1]

facial jaundice is included I think that yellowness of face due to hypercarotinæmia might also be mentioned his condition the sclerotics do not share in the yellowness hey do in true biliary jaundice

nequal pupils resulting from neurosyphilis are of course tioned among the important facial signs. But the ual pupils forming a part of Adie's syndrome (or Markus's drome)[2] have not been included

he "ecchymotic mask, due to accidental violent com sion of the chest wall is beautifully illustrated in French ical literature If the patient survives, I believe the l ecchymoses completely disappear

ethæmoglobinæmia or sulphæmoglobinæmia sometimes e a ghastly tinge to the face but these conditions are not n encountered

he telangiectases of the Rendu Osler type of telangiec may not be obvious in some cases

characteristic examples of Bourneville's disease (tuberous rosis) the tell tale so-called Pringle's nævi (telangiectatic ceous adenomata) grouped about the nose are very king

he combination of the facial vascular nævus with buph lmos ("ox-eye) on the same side and hemiparesis on opposite side of the body is seen in classical examples of the ge Weber Kalischer syndrome

scar in the parotid region associated with flushing and ating on the same side of the face is the least ommon type of the auriculo temporal and allied dromes.[3]

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arkes Weber F *Brit med J* 1939 ii, 466

arkes Weber F *Proc. R Soc Med* 1933, 26, 60

arkes Weber F Rare Diseases and Some Debatable Subjects. London, 1946; pp. 59 66

The presence of even the slightest xanthelasma of the eyelids may I think, sometimes have an important significance because of its occasional association with xanthomatosis of other parts of the body and with grave atheromatous lesions of the cardiovascular system

London N W 1 **F Parkes Weber.**

SIR,—As a non medical reader of the *Lancet* I feel impelled to congratulate you upon Pierrhos StKatsareas's article which has the true note of Sir Thomas Browne in many sentences But alas! that you should speak of Alcmene's nights instead of Alcmena's True that mean ale may make for misery but I believed that you knew Sir Thomas Browne by heart

London S W 1 **F Sherwood Taylor.**

SPUTUM IN CHRONIC BRONCHITIS

SIR,—We should like to comment on the article by Dr Elmes and his colleagues last week

In hospital we see for the most part, the patient with complicated chronic bronchitis. By that is meant chronic bronchitis with emphysema, with right ventricular hypertrophy with congestive cardiac failure, with cerebral anoxia, or in patients acutely ill from a respiratory infection. In other words we begin and end with a respiratory cripple, unemployable or only employable in a limited capacity Dr Elmes's cases are no exception

To pursue the prophylaxis of acute respiratory infections in chronic bronchitis, one would have to enlist the aid of the general practitioner who sees bronchitis in its early stages. The College of General Practitioners could with outside expert help tackle this most important problem The general practitioner in an industrial area (where bronchitis is most prevalent) is very busy in the winter so the antibiotic would have to be given by mouth and here we would plead for chloramphenicol, which is condemned by Dr Elmes and his colleagues We have used it ever since it became available and have not encountered any toxic effects. We give it in divided doses of 2 g daily for not more than six days Its effect in clearing *Hæmophilus influenzæ*, the really awkward infection in our experience, is dramatic We are sure that it has been responsible for saving many lives It does occasionally produce diarrhœa, but this seldom lasts for more than twenty four hours Aureomycin on the other hand can cause distressing diarrhœa and for this reason we have abandoned its use unless it is specifically indicated.

We wonder whether respiratory infections are a major factor in making a respiratory cripple of a chronic bronchitic What about cough and smoking? Is not a mucoid sputum with its attendant cough more injurious over the years than respiratory infection each winter? These infections do not usually by themselves, cause death until later in the disease when the patient no longer has uncomplicated chronic bronchitis In our efforts to eradicate the pathogens from the respiratory tract, it would seem probable that, in the course of a time, the bacterial world will develop a new armour and we will be caught up in the endless game of antibiotic versus bacterium Therefore, whilst not denying that the prophylaxis of the respiratory infection in chronic bronchitics is a most desirable objective surely we must if we are to produce any lasting benefit for these patients, concentrate more on the origin social aspects, and morbid anatomy and histology of the disease We might then be able to define what we mean by chronic bronchitis!

Finally we should like to congratulate Dr Elmes and his colleagues on their thoughtfulness in selecting patients who could attend daily without financial loss The chronic bronchitic comes mainly from the lower income group and in our clinic we make sure that pay is not lost because of the visit

Chase Farm Hospital,
Enfield Middlesex.

Thomas Simpson
F K Westlake

GASTRIC RESECTION FOR HÆMORRHAGE

SIR,—Mr Gordon Ferguson (Oct 10) raises the problem of the correct procedure when no cause is found at laparotomy performed for recurrent hæmatemesis and melæna These cases are usually due to acute gastric ulcers which are impalpable at operation The follow-up of acute gastric ulcers, causing bleeding and diagnosed gastroscopically, gives a clue to the best surgical procedure In men there is a big proportion who subsequently return with chronic gastroduodenal ulcers, and partial gastrectomy is therefore reasonable at a time of brisk and repeated bleeding when no obvious cause has been found, but the surgeon is well advised to inspect the remaining part of the stomach before completing the operation In women the follow-up of acute ulcers is excellent, few returning with chronic ulcers, but there may be further episodes of bleeding [1]

We believe the best procedure is that described by Mr G L Bohn, of Reading He opens the stomach and not only inspects the mucosa for the acute ulcer but palpates for the exposed vessel which may feel like a small hard shot through the rubber gloves Having located the vessel, he then performs an intragastric submucosal resection of the ulcer In this particular group of patients, we think this is a very valuable technique Where available, gastroscopy can be a real help in locating small bleeding ulcers in cases which may require surgery Bleeding tends to recur at intervals of 12–24 hours, and it is sometimes possible to choose a time when bleeding has stopped and when the stomach is empty

Department of Gastroenterology,
Central Middlesex Hospital,
London N W 10

F AVERY JONES
J W P GUMMER

SIR,—In his article on gastric resection for gastroduodenal hæmorrhage without an obvious ulcer, Mr Ferguson mentions the inadequacy of the inspection of the stomach made possible by gastrotomy

May I, in this connection, recall that many years ago Rovsing, in Copenhagen, on such occasions used the simple expedient of introducing a small lamp through the gastrotomy and inspecting the transilluminated stomach wall He stated that by this means the bleeding vessel could be easily found by the interruption in its course, which could be clearly seen He became cautious about the procedure because of some accident with an electrical short-circuit, but this should be avoidable with modern equipment—possibly low-voltage lamps

Berne Switzerland

P LUNDSGAARD HANSEN

Medicine and the Law

Professional Negligence An Unsuccessful Appeal

LAST March a widow was awarded damages in her action against two dental surgeons on the ground that their negligence in the professional treatment of her husband had caused his death One of the defendants extracted teeth from the patient's mouth while the other administered the anæsthetic Somehow the patient swallowed or inhaled a throat pack which had been inserted in his mouth, and asphyxia resulted At the trial the judge took the view that the facts indicated negligence and that it was for the defendants to rebut that indication The Court of Appeal has refused to interfere with his decision [2] The appellants contended that the occurrence was an unfortunate mishap of an extremely rare kind which could not reasonably have been foreseen, the fact that it happened was no proof of negligence Lord Justice Somervell rejected this contention It had been argued, he said, that the two dental surgeons had followed the usual practice of their profession and that a series of highly impr coincidences had caused the patient's death. But was ample evidence to support the finding reached trial court that the throat pack had been too This, said the Lord Justice, called for an and the defendants' attempted explanation had broken down Lord Justice Denning, concurring that the accident was one which could and have been avoided, the fact that a similar had never happened previously was really som which told against the defendants The appeal dismissed and leave to appeal to the House of L refused

It is familiar law that a medical or dental practit while he owes the duty to use reasonable skill and does not guarantee successful treatment any more a lawyer guarantees to win his client's case. not responsible for an accident which could not ably have been foreseen Where the line should drawn—what degree of care and skill is reasona is a question depending on the circumstances of each The ruling of the Court of Appeal, disturbing th it may appear, need not be taken as altering the ge principles of professional liability What is neg and what is an accident will still have to be deci the light of the particular facts established in evidence

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[1] Jones F A King W E Ann Aust Coll Phys (in the press)

[2] Times, Oct. 31 1953

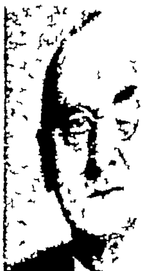
Obituary

WILLIAM NORWOOD EAST

Kt, M D Lond, F R C P

Sir Norwood East, a former Commissioner of P and a director of the Prison Medical Service, died home at Crowthorne, Berks, on Oct 30 He retired active work in the prisons in 1938, but his coll will find the Prison Medical Service strange without for he had never ceased to attend conferences, both and informal, and they had continued to rely on wisdom, experience, and sympathy

He was born in London, on Christmas Eve, 187 son of Mr W Quartermaine East, D L and he educated at King's College School and King's C



He qualified from Guy's Hospital in 1897, and two years later he joined the Prison Service as a medical officer He held appointments at many of the larger prisons before he was appointed senior medical officer at Brixton Prison in the early 'twenties The work of a senior medical officer at Brixton involved spending many days in court, not only at the Old Bailey but in assize towns in the Home Counties Much of the day to day work at the prison had to be done in the evenings after return from court, but East never spared himself His reputation as an expert witness stood high, and he would spend long hours taking a history from a man on mental state the court had asked for a report

In 1924 he became Medical Inspector of Prisons he brought to the Prison Commission a capacity which has seldom been equalled He the provision of an up-to-date operating-thea Wormwood Scrubs Prison, so that major surgical tions could be carried out within the prison, and started the prison nursing service with State-reg nurses He became a Prison Commissioner in 193 he was also appointed director of the Prison Service

Retirement in 1938 brought him little relaxation his hard work He continued to be one of the d appointed by the Home Secretary to inquire into mental state of prisoners on whom the capital had been passed These inquiries often involved journeys at short notice with an exacting and re duty at the end of the journey He also conti ture in forensic psychiatry at the Maudsley Hospital dical School

Ie was an effective and lucid speaker and an active mber of the societies of his specialty and in due rse he presided in turn over the Society for the Study Inebriety and Drug Addiction (1940–45), the psychi ic section of the Royal Society of Medicine (1948) and Medico-legal Society (1945–47) In his books and ays East also made a remarkable contribution to his cialty *Forensic Psychiatry* (1927) is a useful guide doctors called to give evidence in the courts on mental cases. *Medical Aspects of Crime* (1930) is a collection thoughtful essays. In *Psychological Treatment of Crime* 39) he and the late Dr W A. de B Hubert described ir investigation into the psychological treatment of minals and recommended that a special establishment hin the Prison Service should be provided to deal h psychopathic personalities and other psychiatric es. One of the last occasions on which East attended Prison Commission was at a meeting to discuss the nning of this establishment But the start of this ject has been much delayed by post war conditions *ciety and the Criminal* (1949) is another collection essays which he described as some of the stepping nes over which I have travelled towards a better lerstanding of crime and criminals'

C W M recalls that East came as senior medical cer to Brixton Prison from Liverpool Prison with the utation of being a formidable personality and a hard rker

We juniors were told we were in for a strenuous time der him We found him strict but fair and without doubt remendous worker He helped and encouraged us all he ld and from him we learned much. Many young dical officers owe their successful careers to him, and I had the privilege of succeeding him as medical com sioner know it was not only his colleagues he helped ny ex prisoners owe a great debt of gratitude to him for was blessed with sympathetic understanding of their knesses and difficulties, and helped many to overcome m. At the end of his last book he bids those who follow 'be faithful to scientific standards and earn the respect his colleagues East was certainly faithful to scientific ndards and he earned the respect of his colleagues.

J L. writes: Norwood East cannot be replaced psychiatry like his social and moral convictions, solid and simple free from the complex uncertainties t now harass us

This simplicity was not the outcome of unawareness or defect of penetration and grasp With an unrivalled y of experience at his call and an exceptional knowledge he literature of his subject he could give a sure empirical gment on any practical question of forensic psychiatry a wisely critical survey of theoretical issues such as ability His unassuming integrity sense of duty and spoken opinions went with a humane regard for individuals a concern for their betterment which was reflected in advocacy of the therapeutic penal institution He had time for cant or sentimentality he detested vapid excuses criminal behaviour and he had a strong sense of things ible; but he fought with courage and determination what he thought should be done to improve our under ding of the delinquent and our capacity to help him His arch was characteristically thorough and cautious his ting, like his conversation pithy and unequivocal About research he was needlessly modest; his contribution to study of adolescent offenders is a monument that will d. Teaching gave him keen pleasure and he prized the ortunity greatly During the thirty years he lectured the Maudsley he was unremitting in attendance and ful preparation; he gave his last series of lectures only months ago and was lucid and vigorous as ever with extraordinary case memory fully at his disposal.

Looking back, one recalls his slightly formal courtesy humour his genuine respect for the work of others and ove all his outstanding honesty of mind and steadiness of pose Whose life was distinct and in Method and his ions as it were cast up before A man firm and standing his purpose nor heav'd off with each winde and passion that thinkes what he does and does what he sayes, and sees what he may doe before he purposes. A man well d in all humours, in whom nature shew'd most Geometry the has not spoyl'd the Worke

EMMA CHRISTINE PILLMAN-WILLIAMS

M.B.E., M.A. Camb., M.B Lond

Mrs. Pillman Williams chemical pathologist to the Royal Free Hospital, died at her home in London on Oct 28

She came of an old Devonshire family and she was educated at Sidcup and Blackheath High Schools and at Girton College Cambridge where she took the natural sciences tripos specialising for her part II in physiology From Cambridge she went in 1910 to the London School of Medicine for Women After qualifying in 1914 she held house-appointments at the Royal Free Hospital where she later became assistant anæsthetist In 1916 she was seconded to the Ministry of Munitions as chief medical officer at No 7 Filling Factory Here she collected the material for her first paper, which dealt with the aplastic anæmia developed by trinitrotoluene (T N T) workers For her work at the factory she was appointed M.B.E

In 1919 she returned to the Royal Free and its medical school and she worked there till 1923, with a grant from the Medical Research Council, on the chemical changes in blood and urine during pregnancy The importance of these early investigations, and indeed of much of her later work was not fully appreciated for she had little gift for exposition and would sum up the research of years in a paper so condensed that it was barely comprehensible From 1923 to the outbreak of the late war she worked in what became the chemical pathology department of the hospital During this time her interest turned more and more to nutrition and dietetics and with Dr Dorothy Hare she studied the treatment of rheumatoid arthritis by a diet of raw fruit and vegetables with first-class protein and some fats. A film showing the remarkable improvement obtained in some severely crippled patients is still in existence but here again a full account of the investigation was never published Mrs. Williams was an advocate of this diet for people in general. From their early youth her family was brought up on a modification of it, largely prepared by her own hands and the physique of her sons in her opinion put Q.E.D to her theories of dietetics. She was a staunch and critical supporter of the Food Education Society

During the late war she was on whole-time service at the base hospital of the Royal Free at Arlesey but she returned to London in 1940 and was appointed senior lecturer in charge of the department of chemical pathology a post which she held at the time of her death

L. W writes I came late to medicine and it was as a student that I first appreciated Christine Williams's outstanding characteristics—her all-embracing kindness and her interest in her fellow men. It was only her incredible energy and her will power that enabled her to pursue her career while bringing up her family of four outsize sons With her Swiss Family Robinson bag Piller as she was called by her friends was an essential part of the hospital colleagues, residents, nursing staff students, patients all came to her for help and she never failed to respond For every ill there was always a vitamin! She kept open house, first at Cumberland Terrace and later at Harley Street a party of fifty lads for the night was taken in her stride At Arlesey her hospitality her personality and her determination to get on with the job did much for the morale of staff and students alike Her patients adored her and would report for years after their discharge knowing that help and advice would be theirs. In fact everyone came to Christine and I used to describe her as the most imposed-on individual in the hospital Generous to a fault, she would cheerfully give her all and go hungry and in rags. In her youth she was fascinating and pretty with a milkmaid's complexion in later life she still charmed in her famous twenty year-old Paris hat

In 1919 she married Dr Ulysses Williams radiologist to the Royal Free Hospital. There are four sons of the marriage

Notes and News

FROM CARE TO CURE

ON Oct 28 the Duke of Edinburgh visited Goodmayes Hospital, Essex, to see something of its work Speaking at a luncheon afterwards he said "This hospital interested me as an individual, because it is seeing what is really the beginning of a revolution—the revolution from care to cure It strikes me that it must be a source of very great satisfaction to doctors and nurses in this service to know that they are making or doing a positive good in the healing of the mentally sick This is a satisfaction which the rest of the medical profession have had for a very long time but which for the mental health service has only really begun to start"

Mr Iain Macleod, the Minister of Health, said that when it was known that the Duke of Edinburgh wished to visit a mental hospital it had seemed sensible to invite him to one where the staffing situation came somewhere between adequate staffing and an acute shortage, to choose a hospital where overcrowding was neither negligible nor formidable They wanted to show him a hospital where good work was being done in old buildings Goodmayes was typical of many other hospitals of this kind—neither the newest nor the oldest which were "the county regiments of the Army" of those who served in the mental health field

THE HOSPITALS YEAR BOOK

FOR a reference book familiarity breeds affection rather than contempt, and friends of the *Hospitals Year Book*[1] will be glad to find the 1953–54 edition its usual informative self But Mr J F Milnes, the editor, shows discrimination in his respect for tradition and he has sensibly dropped the detailed bed and patient statistics, now largely available in the Ministry of Health's *Annual Review of Hospital and Specialist Services* Thanks to this saving of space he is able this year to give us details of mass radiography units, and to provide a separate index to special hospitals The index to statutory instruments, memoranda, and circulars has been expanded to include N H S Whitley Council circulars and there is also a short bibliography of books and reports about hospitals

SURVIVAL OF CASTAWAYS AT SEA

IN peace time 50,000 persons a year die as castaways, 90% of them from despair in the first three days Dr Alain Bombard[2] believed that a castaway need not die of hunger ("there are nearly two hundred times as many living organisms in a cubic foot of water as in the same amount of earth"), or of thirst (provided his kidneys are healthy an average man can drink with impunity $1^1/_2$ pints of sea water a day), or from despair (because survival is feasible) He read all he could about shipwrecks, the experiences of survivors, the chemical composition of fish and how to catch them, and winds and currents, and he experimented with plankton for food He then set out to prove his case

After a preliminary canter in the Mediterranean Dr Bombard drifted alone for 65 days in an 18 ft inflated rubber dinghy from the Canaries to Barbados For vitamins A, B, and D he relied on fish, and for vitamin C on plankton For water he used the sea and pressed fish He took emergency rations but never opened them He took no sun glasses, but he did take a sextant, fishing tackle, a small parachute to serve as a sea anchor and as a net for plankton, and a small sail, whose most useful functions were catching the rain and acting as a shelter from the sun He recorded daily his blood pressure, his temperature, and the state of his skin, nails, hair, and mucosæ, he measured his urine, and noted his muscular strength and the number of stools passed Among other discoveries he disproved the fallacies that there are no fish away from inshore waters and that sea water is laxative After a month or so enteritis set in, but after 53 days he met a liner and had a small meal, which gave him the worst stomach trouble of the whole voyage but apparently cured his enteritis During the voyage his blood pressure varied with his state of mind, both being depressed together, the meeting with the liner restored both to normal After leaving the liner he continued for another 12 days before landing in Barbados By this time he had lost 55 lb in weight and 2 500,000 red cells per c mm of blood, but he showed no signs of
deficiency

It may be objected that whereas Dr Bombard was used to roughing it at sea, other castaways might to seasickness or be otherwise incapable of keeping th alive as he did But by enterprise and endurance he ha his point and has made it in a way that must cause attention to be given to the needs of survivors from th

BEER BY THE REED

SOME take their vitamin B in wholemeal bread, the husks of their rice, some buy it in a pot or a have it for breakfast, but the 16,000 inhabitants of Island, in Lake Victoria, take it as—and at—a beer The island measures 30 square miles, and when decides to hold a beer drink everybody, in theory, can Fortunately only about 200–400 of the nearest usually turn up

Dr Hope Trant, who describes one of these social in the East African Medical Survey Annual Report[1] says, that the men arrive first, usually at about 4 P.M., carrying a drinking reed, and most of them bring own stools Those without stools look round for sit on, if necessary supplying themselves from the foundations of the huts Meanwhile the men of the hou which is offering the beer are boiling up water in aluminium saucepans, called sufurias, which have used to make the porridge for dinner They have not washed since, so the water is nourishing and scummy

The beer itself is already prepared and stands in large earthen pots The recipe for brewing it is complex, and by our standards original

> First take a measured quantity of red sorghum (Guinea corn) and put it in a large wooden trough, add water for eight hours Mix with ashes and spread on a flat rock with grass and leave for 1–2 days to germinate When begins, wash to remove ashes, dry in the sun and grind known as *kimela* Place flour in the trough and mix with leave 3–4 weeks, turning with a wooden shovel every 2 or Next shovel on to a corrugated iron sheet and heat over turning with a wooden shovel all the time until it is hard blackish lumps like small pieces of coke Complete in the sun This product is called *kongo*, and will keep
>
> Repeat the recipe for making kimela, but using millet of sorghum. Measure out equal parts of kongo and millet Put a little of the millet kimela into the bottom of an ware pot, and add a 4 gallon tin of kongo mixed with water for 36 hours Mix the remaining millet kimela with water to pot containing kongo ferment. Leave for 4 hours, when will be ready to serve It is pinkish, tasteless, and heady

The visitors, while waiting for refreshment, groups and talk at the tops of their voices or draw water from the sufurias through their reeds, to that they are not blocked by the dregs of earlier As the scummy water comes to the boil they begin to round various hollows in the ground where the beer are to be placed One of the family comes along with deepens the holes, which are about 2 ft deep and Now the seats are placed round the holes until about 50 people, in three or four rows, round each talking loudly, with their tall reeds, tipped with forated tin cones which act as filters, pointed like the sky These reeds may be as much as 6 ft long, valued possessions, some are carried round, like in hollow containers, and extracted with pride and The longest reeds, as Dr Trant points out, are adapted to back benchers

Now the woven beer baskets, each capable of holding gallons, are brought along and patted into their pl the holes by willing helpers The hosts reckon that need 4 gallons for a 12 hour drink. Out comes the its 6 gallon earthenware pots, two staggering carried each, and someone thrusts his hand in to give the brew stir, his arm comes out coated to the shoulder with looks like bran mash The beer is poured sloppily, like gruel, into the baskets until they are half filled, and stage some rowdy spirits produce gourds and try to a little, shouts and cries from the other guests d this bad form The water boilers now arrive, carrying hot sufurias with bunches of green leaves, and the are filled to the brim for in Ukara beer is drunk warm diluted If there is not enough water to fill the bask has to be fetched from the lake and boiled, so waiting one's beer is a severe test of manners. Nevertheless ts (except perhaps an elder who may take a suck or two pretence of testing the flavour) until the host gives the al. It is a silent signal hard to detect but in a nent the reeds pierce the brown scum and the beer drink ns.

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[1] Published by the Institute of Hospital Administrators 75 Portland Place London W 1 1953 Pp 1088 42s

[2] The Bombard Story André Deutsch, London 1953 Pp 214 12s 6d

[1] Published by authority of the East Africa High C Kenya The English Press Pp 74

usually lasts, Dr Trant says, from 6 P M till 4 next ning and when the men have finished fresh hot water is red on the dregs and the women have a turn If there is ugh beer left over the same people come back next day finish it There is no drunkenness, however Those reach the swaying stage are discouraged from a further ion, and those who become too uproarious are sent home the end of the party everyone is able to walk home to bed riety is also favoured by the fact that sucking up beer ough a long reed is hard work

nly the chief and one or two headmen drink beer every but even ordinary people manage to get to a beer k about once a month A stranger has to pay 5s to headman of his area when he arrives, so that he will be epted as one of the family when he goes to a beer drink otherwise there is no charge This single entrance fee kes him welcome at all drinking festivities on Ukara.

eer making certainly uses up grain which might be kept food but on the other hand, its yeast content is an ortant source of vitamin B Moreover the inhabitants Jkara are exporters of rice and cassava; they can afford be a little extravagant in pursuit of their favourite eation.

MORE FLOWERS BY REQUEST

the long ago days when boating was the thing the ames lock keepers held an annual flower-growing competi n. Perhaps they still do At all events those always sunny mers are marvellously coloured and scented in memory their brilliant triumphs Country stations, too contend in way spilling lobelia and nasturtiums prodigally among coal-stacks, and training ramblers along the palings, to great refreshment of travellers Now the Worshipful npany of Gardeners and the London Gardens Society (20 kingham Street, W C 2) are striving to rouse the same ticultural spirit in the hospitals, beginning in a small way h the postgraduate and undergraduate teaching hospitals the London area. This year sixteen hospitals competed, l there is every hope that next year more will join in. perpetual silver cup presented by the company was won the Middlesex Hospital the silver and gilt medals, presented the society by St Luke's Woodside Hospital and the dsley Hospital respectively and certificates of merit by London Hospital and Queen Charlotte's

With this example before them other hospitals should pick their spades. The object of the competition is to encour the use of flowers *supplementary* to those at present usually nd in the wards, and the judges take into account not y the extent to which available open spaces are cultivated embellished and the decorative effect produced by ers in window boxes, waiting rooms, and corridors, but the skill of the gardeners in overcoming such drawbacks poor sites and little sun and the arrangement of plants provision for a succession of blooms On two unspecified es between April and October they call to see what is going Hospitals must thus keep on their mettle and not yield the gardener's temptation to murmur with Ruth Draper: ou ought to have seen it last week.

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iversity of London

On Sept 30 the following degrees were conferred

M D—Helen Ingleby
M S—F B Cockett

iversity of Aberdeen

On Oct 8 the following degrees were conferred:

Ch M—G E Mavor
M B, Ch B—Frances Allan J G Barnett G R Buchan, C Coutts, B B Dale N I Edmond J D Garden, Walter les, J D Johnston Donald Macintosh James McNab O O rrer, A N Milne V J Murphy, G G Rennie T F Rennie F Stewart, J V Watt, Isobel M Wood

iversity of St Andrews

Dr A. Greig Anderson is one of the five commissioners pointed under the University of St Andrews Act 1953 reorganise the university in accordance with the recom ndations of the Royal Commission in University Education Dundee

University of Liverpool

Prof Rudolph Nissen, of the department of surgery University of Basle will deliver the William Mitchell Banks lecture on Friday Nov 13 at 5 15 P M. at the medical school He is to speak on the Romance of Thoracic Surgery

Royal College of Physicians of London

At a comitia of the college held on Oct 29 with Sir Russell Brain the president in the chair, Dr T Jenner Hoskin Dr B E. Schlesinger Dr A. M Cooke and Dr J C Hovle were elected councillors; Dr J Forest Smith was elected representative on the Committee of Management and Sir Russell Brain Sir Harold Boldero Dr W G Barnard Sir Allen Daley and Dr A M Cooke were re-elected members of the Standing Joint Committee of the three Royal Colleges. Dr J A Smiley was appointed Milroy lecturer for 1955

The following candidates were elected to the membership:

Youssef Kamel Wasfi Aboul Dahab M B. Cairo Mary H Aitken M.D Edin. Mary Bateman, M.D Lond., D B Benaron, M.B. Lond. R A Bruce B.M Oxfd, William Brumfitt, M.B. Lond J I Caley M B. Sheff Rosemary A Cooper, M.B. Camb, R. F A Dean, A E Dormer M.B. Lond. C. I V Evans, M.B. Sydney J H Evans M B. Lond Henry Foster M B. Lond., major R.A.M.C. Louis Friedlander M.B. Witwatersrand J F Hale B.M. Oxfd, D R. Hay M B. N.Z. F E. Higgins, M B. Birm. A. W. Johnston M B. Camb F N M. Johnston M B. Camb., Lilian F Jones, M.B. Birm. H I Lambert, M B Camb, Graeme Larkins, M.B. Melb J C Leonard M.D Lond Adib Zaki Abd El Masseh M B. Cairo B F Robinson M.B Lond. Albert Sachs, C.B.E., M D Dubl brigadier R.A.M.C. Q.H.P., A W Steinbeck M B Sydney L. V Sthyr, M D Lond J D Stride, surgeon lieutenant-commander R.N J H. Tyrer M.D Sydney B W Webb M.D Lond

Licences to practise were conferred on the following 106 candidates who have passed the final examination of the conjoint board:

John Anderson M E. Anfilogoff Christine M Armstrong B S Beardsworth P J Bell J A Bevan, Cecil Bishop R. J Blow C W W Brown L. F Brunt, J D Campling Patricia M. Carpenter J A A. S Chamberlain Webber, H J Clarke, Alan Clark Jones, W F Clifford-Jones J T Coals R. J C Cobbold, C W M Cooper Violet G Cousins Shirley A. Crockatt John Crook, L D Davies, W C. Davies, Jose A Day J D Devitt, Eva M Dilling M S. G Douglas, D R. Elam, J L Evans Paul Field, C. V Foll, Gillian France P J Frost Thomas Gibson Lawrence Goldie Rosemary A Grange A N Green J M Green, F V Griffiths Sripal Tilak Gunewardene Dorothy J Harden, Margaret M. Heley E. J Hill, Harold Holden, W J Jackson, Elsie Jaques, L R. Jenkins, J J Jones, Elizabeth M. H. Kennett, Paul Konfortion, G E T Lawley I V Lishman, David Longbourne, Kypros Loucas, T M McAneny J G Macdonald, M. A. McDonald, G F Mackenzie T D M McNeill Patricia S Matthew Bridget d E. Matthews, Clifford Mawdsley, Jean E Moffat, Margaret L. M. Monro R. J Morgan, F J Morley, C E Nelson M R. Oates, R. C. Oliva, Patricia M. O'Sullivan R. B Pardoe D J Parry, D M Paul, J D W Peck, J W Prout, J E G Rault, A D Richardson, J A V Riley, A A Roe W A St. John S C C. Scott, D E Sharland Jean M. Shields A J Slim, Marguerite L. Sloper P C Smart, C. J Stephens R. L. G Sutcliffe G W. Sykes Michael Tack, Andrew Talalla, R. W H Taverner E M. Thomas, C. P D Tong, E. A M. Tuck, H M Turner, J. C S Turner F R Valentine Hagart, H W C. Ward, Isabel M P Ward W H. Waters J H H. Webster P H. Wiesendanger Lee Yoke Htyan, G W G Yule

Diplomas were conferred on those named in the report of the meeting of the Royal College of Surgeons in our issue of Oct 17 (p 841) The following diplomas were also conferred:

D M.R. D—Kirikankanange Mahendrapala Chandrasena de Silva, Habaraduwa Kudabokola Teelon Fernando P G, Keates Leonard Langton, Kee Loo Lim, E A H MacLaughlin O D Macnamara W B D Malie Ambika Charan Mitra Bernard O Hare A W Robinson Amalendu Roy Hussain Tayebbhoy J A Watson
D C.H—Elizabeth A Martin, K R. Momberg.
D.M.R T—D M T Cones, G McK. Crawford D, A L. Dick, Marjorie O Dunster G B Goodman, B T Hale, F E. Neal, J D Reeves Mohammed Samiullah J G Stewart Elsie N K. Wallace
D O—J M. Ferries.

British Association of Physical Medicine

The annual meeting will be held at King's College Hospital, London, S.E.5 on Friday and Saturday April 30 and May 1

Germ free Life

We published last week (p 933) an account of the work of Prof J A Reyniers on the rearing of germ free animals Professor Reyniers described his technique and results at a meeting in London on Oct 15 arranged by Dr W P Blount poultry adviser to the British Oil & Cake Mills Ltd.

Myxomatosis

The Ministry of Agriculture and Fisheries report that myxomatosis has been found among wild rabbits near Robertsbridge in Sussex The area involved covers woodland of about 100 acres The disease was confirmed among rabbits near Edenbridge in Kent two weeks ago (see *Lancet* Oct 31, 1953 p 935) The *Manchester Guardian* (Nov 3) reports Prof G Ramon (Pasteur Institute) as saying that the disease has spread into Germany Belgium and Holland

Royal Appointment

Captain J B Oldham, R N V R, has been appointed an honorary surgeon to the Queen, in succession to Captain G McCoull, R N V R

Charterhouse Rheumatism Clinic

Dr J F Brailsford will deliver the Gilbert Scott lecture on Thursday, Nov 19, at 5 P M, at the clinic, 56, Weymouth Street, London, W 1 He will speak on the Prevention Detection, and Treatment of Osteo arthritis

Nichols Fellowship

The council of the Royal Society of Medicine invites applications for this fellowship, which takes the form of a grant of £225 per annum in aid of research in obstetrics and gynæcology Applications should be made before May 15 to the secretary of the society, 1, Wimpole Street, London, W 1, from whom further particulars may be had

Shortage of Resident Staff

The latest annual report of the Mansfield Hospital Management Committee expresses concern at the difficulty in obtaining resident doctors, particularly for the casualty and anæsthetic services The salaries paid to such doctors are " certainly no inducement to remain in the service longer than the 12 months' statutory period after qualifying " For many years, the report adds, the almost traditionally low salaries have been accepted, but now a new approach should be made to the question of the remuneration of young resident doctors

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Dr Willi Hoffer has been appointed to the Abraham Flexner visiting lectureship at Vanderbilt University, Nashville, Tennessee

Diary of the Week

NOV 8 TO 14

Monday, 9th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road W 12
4 P M Prof G W Pickering Concept of Essential Hypertension

ROYAL EYE HOSPITAL St George s Circus S E 1
5 30 P M Prof Thomas Nicol Surgical Anatomy of Orbit and Ocular Adnexa.

MEDICAL SOCIETY OF LONDON 11, Chandos Street W 1
8 30 P.M Mr E S Horning, B.SC Sir Stanford Cade Hormones in Relation to Cancer

Tuesday, 10th

ROYAL COLLEGE OF SURGEONS Lincoln's Inn Fields W C 2
3 45 P M Mr W H Jayne Slide Culture of Malignant Cells (Erasmus Wilson demonstration)

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical Medicine Keppel Street W C 1) Prof E J King PH D Alkaline and Acid Phosphatases

ROYAL SOCIETY OF MEDICINE 1 Wimpole Street W 1
8 P.M *Section of Psychiatry* Dr J H Gould Use of Vitamins in Psychiatric Practice

ROYAL EYE HOSPITAL
5 P M Mr T M Tyrrell Pitfalls in Refraction

INSTITUTE OF DERMATOLOGY St John s Hospital Lisle Street W C 2
5 30 P.M Dr D O Neill Stress in Relation to Diseases of the Skin

WEST END HOSPITAL FOR NERVOUS DISEASES 40 Marylebone Lane W 1
5 30 P M Mr G C Knight Spinal Compression

CHELSEA CLINICAL SOCIETY
8 30 P M (South Kensington Hotel 41, Queen s Gate Terrace S W 7) Mr F E Henderson, A M I E E Dr Phillippe Bauwens Electronics in Industry and Medicine

MANCHESTER MEDICAL SOCIETY
8 P.M. (Medical School University of Manchester) *Section of Surgery* Mr W F Nicholson Surgery of Pulmonary Tuberculosis

Wednesday, 11th

SOCIETY OF APOTHECARIES OF LONDON Black Friars Lane E C 4
4 P M Prof C H Gray Fluid and Electrolyte Balance
5 15 P M Mr F A Williamson Noble Early Treatment of Eye Diseases

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P M Dr H Bickel Observations on Lignac Fanconi Disease Wilson s Disease and Phenylketonuria

ROYAL SOCIETY OF MEDICINE
4 30 P M *Section of Physical Medicine* Dr Michael Kremer Acroparæsthesia and Costo-clavicular Compression
8 P.M *Section of Proctology* Mr T McW Millar John of Arderne the Father of British Proctology (Presidential address)

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE 28 Portland Place W 1
3 30 P M Dr J Greenwood Wilson Care and Aftercare—the Cardiff Interpretation

INSTITUTE OF DERMATOLOGY
5 30 P.M Dr H Haber Benign Epithelial Tumours of Skin

BRITISH ASSOCIATION OF SPORT AND MEDICINE
5 P M (Westminster Medical School Horseferry Road S W 1) Dr H Noel Bleasdale Health and Minor Maladies of Swimmers and Divers Dr Michael Ward Medical Aspects of the Everest Expedition, 1953

MANCHESTER MEDICAL SOCIETY
4 30 P.M *Section of Pathology* Dr F A Langley Ova Tumours—Human and Experimental.

MEDICO CHIRURGICAL SOCIETY OF EDINBURGH
8 30 P M (Royal College of Surgeons, 18, Nicolson Street, E burgh) Dr A S Henderson Dr R E Verney Pro of Student Health (Joint meeting with Royal Me Chirurgical Society of Glasgow)

Thursday, 12th

ROYAL COLLEGE OF PHYSICIANS Pall Mall East, S W 1
5 P.M Prof E J Wayne Diagnosis of Thyrotoxicos shaw lecture)

ROYAL COLLEGE OF SURGEONS
5 P M Mr Geoffrey Keynes Investigations into Disease and Tumour Formation (Cecil Joll lectur

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical Me Mr R L M Synge F R.S Principles of Chromatog

ROYAL SOCIETY OF MEDICINE
5 P.M *Section of Ophthalmology* Dr Karl Hruby (V Clinical Investigation of the Vitreous Body

ROYAL ARMY MEDICAL COLLEGE, Millbank S W 1
5 P M Dr M T Morgan Modern Developments in Rodent and Insecticides in Port Health and Quarantine Ad tration

INSTITUTE OF CHILD HEALTH AND INSTITUTE OF NEUROLOGY
5 30 P M (National Hospital Queen Square W C.1) Dr Dimsdale Syndromes Involving the Basal G Clinical Types Diagnosis and Treatment

INSTITUTE OF DERMATOLOGY
5 30 P.M Dr R W Riddell Pathogenesis of Tinea Capitis

HONYMAN GILLESPIE LECTURE
5 P M (University New Buildings Teviot Place, Edin Prof John Crofton Chemotherapy of Pulmon culosis

Friday, 13th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P M Dr L G Pugh 1953 Everest Expedition.

INSTITUTE OF DERMATOLOGY
5 30 P M Dr O Neill, Dr G B Mitchell Heggs Neur toses

OSLER CLUB OF LONDON
7 45 P M (11 Chandos Street W 1) Prof Ludwig Ed PH D Karl Sudhoff (born Nov 26 1853) Pr Trueta Michael Servetus (died Oct 27, 1553).

UNIVERSITY OF LIVERPOOL
5 15 P M (Medical School) Prof Rudolf Nissen (Basle) E of Thoracic Surgery (William Mitchell Banks lect

Saturday, 14th

BIOCHEMICAL SOCIETY
11 30 A M (St Mary s Hospital Medical School, Padd W 2) Scientific Papers

Appointments

HIRD GORDON M B Aberd D.P H. asst M O H., Wa County Council

JONES CRICHTON M R C S D P H asst M O.H., War County Council

McGOVERN JAMES M B Glasg D P H asst. M O for Salop Council and M O H for Ellesmere urban and rural We and rural and Whitchurch urban districts

Colonial Service:

ASHMORE J H, M B Dubl M O Falkland Islands.

BOWMAN R K M R C.S M O Fiji

CUNNINGHAM A J M B Lpool M O Zanzibar

HARDING H A M D Malta PH C M O Federation of N Nigeria.

HORN D W M.B Edin D T M &H D.P H medical stat

JEFFREYS T E M.R C S M O Federation of Malaya.

MURRAY R J M R C.S resident M O Kenya.

PHILLIPS G A M R C.S M O Federation of Malaya.

YAP POW MENG M.R C S D.P M specialist (psychiatric Kong

Appointed Factory Doctors

DAVIDSON A D O B E M B Aberd for Steyning S

PARKES G S M B Belf for Berkeley, Gloucestershi

WARD C W M.B Leeds for Pateley Bridge, Yorksh

London Transport

EVANS D M M B Camb officer in charge of the n division medical centre Manor House

EYRE J L M B St And D P H D I H senior M O. with of the medical examinations branch Griffith House

SEFTON MYERS C F M B E M R.C.S officer at the nort division medical centre Manor House

South-Western Regional Hospital Board

ARTHURS G N M B Lond F R C.S senior registrar in su surgery Frenchay Hospital Bristol.

CUTHILL, J M M B Glasg D P.M senior registrar in p Tone Vale Hospital, near Taunton Somerset

DUTTON J E M M B Durh, F R C.S registrar in s surgery Frenchay Hospital Bristol

FOREMAN J M M.B N Z, F R C.S E surgical reg Gloucestershire Royal Hospital

JOYCE M H B M B Brist registrar in psychiatry mental hospitals

MORGAN JEAN M.B Brist registrar in pathology, Bath of hospitals

STAGER C P M B B.SC Wales registrar in psychiatry mental hospitals

REATMENT OF ASPHYXIA NEONATORUM

JOSEPHINE M LORD
M.B Lond., M R C P, D C.H
LUNTARY RESEARCH ASSISTANT DEPARTMENT OF OBSTETRICS AND GYNÆCOLOGY HAMMERSMITH HOSPITAL FORMERLY NEONATAL REGISTRAR, HAMMERSMITH HOSPITAL

B W POWELL
M.B Camb M R C P D C.H
SISTANT TO PROFESSOR OF CHILD HEALTH UNIVERSITY OF LONDON

HILDA ROBERTS
M R C.S F.F.A R C.S D C.H
CTURER IN ANÆSTHETICS POSTGRADUATE MEDICAL SCHOOL OF LONDON

SINCE it was advocated by Flagg in 1928, endotracheal ygen has been used in many hospitals for the treatment asphyxiated newborn infants During the last twenty o years, however, so many other methods and appara ses have been introduced that it seems worth trying to aluate the technique of resuscitation as it has evolved Hammersmith Hospital, and to make some comparison our results with others which have been published may be said at once that it has not been possible to ow statistically that any one method is better than other This could not be done without a large ntrolled series a condition which presents almost superable difficulties in problems of this sort

In 1952 O Brien and Roberts, in a short communica m from this hospital, published the results of resuscita m by endotracheal oxygen of 65 asphyxiated infants, phasising particularly the satisfactory mental state the survivors We give our results here in greater tail, with an analysis of the cases by birth weight and d our experience during the last twelve months

The cases studied are those treated during the four ars from February, 1949 to the end of 1952 During e last year of this period three innovations have been ade in our treatment: immediate pharyngeal aspiration babies delivered by cæsarean section; gastric oxygen premature babies and the use of augmented piration whereby the infant s own respiratory efforts e assisted (Donald and Lord 1953) The place of these ethods in our routine is discussed

The study is entirely clinical. No pressure measure ents were made during intubation and the cases have en assessed without reference to X ray appearances, irometry or oxymetry

Endotracheal Oxygen

This method is generally accepted as an efficient means maintaining an airway and of obtaining some oxygena on of the blood by absorption through the bronchial ucosa. There is, however doubt about two aspects of e treatment, namely, its safety and its ability to assist tively in lung expansion Bloxsom (1951) stated that e risk of trauma is so great that tracheal catheterisa on is associated with a considerably increased mortality d that occasionally the lung or the stomach is punc tured; he recommended that the treatment should be bandoned THE LANCET (1951) described the pressures 5 cm. H_2O) as sufficient to allow bronchial absorption of ygen but condemned any attempt to promote lmonary expansion by blowing gases into the achea.

This condemnation springs from the customary state ent that, after attempted lung inflation those cases hich come to necropsy show distension of the bronchioli d alveolar ducts, with complete non-expansion of the lveoli. However, these are in fact post mortem findings when immature lung has been subjected to ante mortem inflation O'Brien and Roberts (1952) stated that the lungs of full time infants could be satisfactorily expanded post mortem, and we have since confirmed their findings in a full time stillborn infant intubated immediately after delivery Day et al (1952) using excised animal material, were also able, by using appropriate cycles of positive pressure to inflate the full time lung and to obtain expansion that was macroscopically and microscopically normal; they failed to expand by positive pressure the lungs of very immature fœtuses. It is therefore possible that endotracheal insufflation can help to expand the lungs of a full time infant, as well as providing oxygen and stimulating the stretch reflex of the lung

When an infant has been successfully revived with endotracheal oxygen it is impossible to estimate to what extent its lungs were expanded by its own efforts, and how much mechanical aid it received and to what areas of the lung The effectiveness of the method must be judged by the clinical improvement seen in individual cases, and from the over all mortality and morbidity figures

Method

This has already been described by Roberts (1949) and O'Brien and Roberts (1952) The following are the essentials

After a vaginal delivery as soon as the baby's head is delivered its mouth and pharynx are aspirated with an electrical sucker Since May 1952 immediate suction has also been used for babies delivered by cæsarean section, the extension from the electric sucker set at a vacuum pressure of 5 in Hg being to hand on the theatre trolley When delivery is completed, the baby is held up by its feet and subsequently nursed head low to promote drainage Where there is moderate asphyxia aspiration is repeated and a small metal airway (Waters no 00) is inserted The baby is next rocked in an oxygen box (Roberts 1949) If there is no response to this treatment within five minutes an endotracheal tube is inserted

In severe asphyxia where the infant is limp where there has been evidence of serious intra uterine anoxia or of aspiration of liquor intubation is performed immediately without preliminary rocking

With the help of a small laryngoscope a no 00 Magill endotracheal tube is introduced through the glottic opening until about $^1/_2$ in lies within the larynx and trachea. The tube is attached to a Y shaped metal connection and oxygen is supplied at $1^1/_2$ litres a minute through the smaller of the two arms If spontaneous respiration does not start the open end of the Y piece is occluded with the finger for not more than two seconds at a time and at the rate of 12–15 times a minute

If the tube becomes occluded with thick mucus it can be used as a sucker being withdrawn while a gentle negative pressure is maintained and then replaced if necessary. Thinner material may be aspirated through a fine Polythene tube passed inside the endotracheal tube

After a cæsarean section a single gastric suction [illegible] once respiration has been established (Gellis et a [illegible]

Gastric Oxygen

As described by Akerren and F[illegible] the administration of gastric oxygen may [illegible] the blood sufficiently to enable the [illegible] of the asphyxiated infant to recover and [illegible] respiration. We have no experience of gastric oxygen [illegible] full time infants, but we believe it is a [illegible] of the treatment for premature infants who [illegible] from complet initial apnœa

During the last year [illegible] insufflation [illegible] therefore been reserved for full time babies [illegible] larger premature babies. For small premat[illegible] gastric oxygen is used. This is administe[illegible] 1 mm. polythene tube attached by a [illegible] the [illegible] the oxygen [illegible]

Dr. Robert Hells Library
[illegible]

TABLE I—INFANTS INTUBATED

—	Survived	Dead	Total
Full time	42	3	45
Premature	18	9	27

0 25 litre a minute An underwater escape valve may be used No "outlet" gastric tube is necessary Stimulant drugs seem to be of some value if the baby is depressed by sedatives or anæsthetics administered to the mother Coramine 0 25–0 50 ml intravenously is used *

Results of Endotracheal Insufflation

In 1949–52 there were 7407 live births, and 72 infants were treated by intubation within a few minutes of delivery, 27 of these were premature (weighing $5^1/_2$ lb or less), and 45 were delivered at term (table I)

FULL TIME INFANTS

45 were intubated and 3 died In addition to these, 9 infants who died of asphyxia were, for various reasons, not intubated Details of the method of delivery are given in table II The majority were delivered by cæsarean section In 6 of the cæsarean-section cases and 2 of the forceps deliveries there was severe maternal pre eclamptic toxæmia

TABLE II—METHODS OF DELIVERY (FULL TIME INFANTS)

Method of delivery	Survived after intubation	Died after intubation	Died without intubation	Total
Cæsarean section	30	0	2	32
Forceps	6	0	1	7
Breech	1	1	0	2
"Normal delivery"	5	2	6	13
Total	42	3	9	54

There was thus a total of 12 asphyxial deaths in full-time infants out of 7407 live births (full time and premature) or 1 6 per 1000 live births The neonatal death-rate from all causes in the hospital during the same period was 21 7 per 1000, hence asphyxia in full-time babies was responsible for just over 7% of the total neonatal deaths Asphyxia was responsible for 12 out of 56 deaths in full-time babies

In this hospital endotracheal intubation is only used for the treatment of severe asphyxia The 9 infants who died without intubation were obviously severe, but for various reasons the treatment was not applied. In six cases an error of judgment was made in the initial assessment of the case which appeared to be borderline or moderate at birth; in others there was a failure of organisation or of technique The lesson we have learnt is that in cases of "borderline" severity it is better to intubate before it may be too late Table III shows details of all the infants who died, and the case histories which follow illustrate some of these points The latter are cases that occurred during the last twelve months of the survey, and were observed personally The table shows that all 3 infants who died in spite of intubation had extremely severe asphyxia and were intubated rather late In case 1 the initial response to intubation was poor The 2 other intubated babies died later from complications of asphyxia neonatorum When asphyxia has been prolonged or severe before birth, the outlook with any form of treatment is bad, but immediate endotracheal aspiration and oxygenation gives the best chance of survival

TABLE IV—PREMATURE BABIES INTUBATED

Birth weight (lb)	Survived	Died	Total
Less than 3	0	2	2
3–4	3	4	7
$4–5^1/_2$	15	3	18

Case 4—Birth weight 10 lb 10 oz Vertex presentation with shoulder arrest The baby was limp and apnoeic at birth, but the cord was pulsating After three minutes the baby was rocked in oxygen, but there was no respiration Intubation was not done until 10 minutes, but the infant was dead At necropsy there was complete atelectasis of the lungs

TABLE III—FATALITIES (FULL-TIME INFANTS)

Case no	Whether intubated	Age at intubation (min)	Comments	Clinical notes	Necropsy findings
1	Yes	10		Forceps, white asphyxia followed by gasping respiration died at 6 hours	Scattered areas of aeration lungs
2	Yes	10		Breech, white asphyxia respiration took 45 min to establish, convulsions after 24 hr, died at 3 days	Congested lungs and lungs floated
3	Yes	10		Cord round neck severe asphyxia, died at $15^1/_2$ hr	Scanty aeration inhalation pneumonia
4	No		Failure of organisation	Shoulder arrest, no spontaneous respiration, died at 10 min (see text)	Complete atelectasis
5	No			White asphyxia rapid onset of cyanosis at 24 hr died at 2 days	No necropsy
6	No		Borderline case	Forceps, cyanosed from birth, died at 48 hr	Atelectasis
7	No			Rapid delivery white asphyxia, died at $2^1/_2$ days	No necropsy
8	No			Rapid delivery, white asphyxia, died at 2 days	Bilateral aspiration pneumonia
9	No		Failure of organisation	Cyanosed since birth Improved on oxygen sudden collapse and death at 18 hr	Pneumothorax many subpleural bullæ
10	No			White asphyxia died at 20 hr	Atelectasis, ? hyaline m
11	No		Borderline case	Cæsarean section antepartum hæmorrhage, white asphyxia, improved spontaneously at first, but died at 24 hr	Bilateral atelectasis
12	No		Borderline case	See text	Bilateral atelectasis, membrane

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* Since this was written we have been tremendously impressed by the value of *N* allyl normorphine hydrobromide (nalorphine hydrobromide) as an antidote to morphine given to the mother

TABLE V—COMPARISON OF RESULTS

Reference	Neonatal deaths per 1000 live births	Neonatal deaths due to asphyxia
ter and Adair (1943)	20·4	18%
istrar-General (1949)	19·3	17%
nty of London (1950)	16·9	21·6%
cher and Rogers (1951)	26·1	34·0%
pé and Pallin (1951)	13·8	—
mmersmith (1949–53) (present rks)	21·7	7%

several other full time infants, apparently equally oked at birth recovered after immediate intubation re most severely asphyxiated infant to survive was a ge premature infant

ase 13 —Birth weight 5 lb 6 oz Delivered by cæsarean tion at the 38th week for severe fœtal and maternal distress n accidental hæmorrhage Fœtal heart rate 70 before tion Liquor heavily bloodstained Infant gasped once a nute after delivery Thick blood aspirated from pharynx dotracheal intubation was done but tube became blocked h blood and was withdrawn 3 ml of blood aspirated from nach. Gastric oxygen given with no improvement dotracheal tube replaced at 5 minutes No improvement on tious intermittent pressures, baby gasping about once a nute. Given both continuous endotracheal and gastric gen for 2 hours Became pink at 15 minutes, and was thing regularly at 2 hours. Hæmorrhage into lungs and nach at 40 hours Given fresh blood transfusion Progress n uneventful Apparently normal at one month Sub ently did not attend follow up clinic

This case illustrates the benefit that may be derived a moribund asphyxiated infant when endotracheal gen is promptly administered Positive pressures e considered dangerous in this case owing to the norrhage In many other cases in which intermittent ufflation with oxygen was used the response has been re rapid and expansion of the chest wall was noted h each insufflation

The decision whether to intubate in a borderline e is a recurrent problem. No such infant who been intubated has died or has shown signs of pul nary or mental damage Case 12 illustrates this blem

ase 12 —Birth weight 6 lb 8 oz. Cæsarean section for ht antepartum hæmorrhage unaccompanied by fœtal ess. Pharyngeal suction not done on delivery Baby eared to have inhaled liquor but cried immediately ryngeal suction done at 2 minutes Baby then became ple and pale but as she gasped irregularly at 7 minutes was not intubated She breathed regularly at 10 minutes ough she was still pale Atelectasis persisted becoming e at 7 hours Intubation was done at 10 hours and gen given at positive pressure with no improvement mented respiration was then tried but after temporary rovement she died at 17 hours Necropsy showed hyaline nbrane

PREMATURE BABIES

Experience has taught us that endotracheal intubation not a satisfactory treatment for small premature ies, but in selected cases where the birth weight is r about 4 lb., it may be of value In our series there e 18 babies who survived this manœuvre Table IV es the number of those who were intubated

Small *premature babies*—Endotracheal insufflation oxygen is regarded as a satisfactory treatment of tial apnœa in larger babies Small premature infants ally attempt to breath shortly after birth unless it been necessary to give the mother large doses of atives or anæsthetic In our experience these few holic premature babies respond badly to tracheal heterisation One such case occurred in the last ar

Case 14 —Birth weight 3 lb 4 oz. Cæsarean section for ere pre-eclamptic toxæmia No spontaneous respiration so baby was intubated at 5 minutes. It immediately became severely shocked and died at 20 minutes in spite of augmented respiration

It was felt that the manipulation of catheterisation contributed to the death of this infant

LATE INTUBATION

Where atelectasis persists several hours after birth whether in full time or premature infants delayed intubation has been found to be an ineffective treatment. These infants are no longer flaccid, and the passage of a tube is more difficult and may cause shock Moreover in these cases any inhaled material will have reached the deeper part of the lung and aspiration of the main bronchi yields nothing The risk of trauma in these circumstances is increased.

SUMMARY OF IMPRESSIONS

Endotracheal suction and insufflation of oxygen form an effective treatment for the initial apnœa of full time infants and large premature infants We consider intubation in very severely asphyxiated infants to be life saving In moderate cases intubation is favoured if progress is unsatisfactory after 5 minutes In cases of borderline severity or suspected inhalation of amniotic material our experience has taught us to favour immediate intubation rather than to wait the routine 5 minutes This is especially important in babies delivered by cæsarean section who are most likely to develop hyaline membranes We have seen no case of hyaline membrane in full time babies that were normal at birth All have had clinical signs of atelectasis persisting and increasing from the moment of birth Until the cause of secondary atelectasis and hyaline membrane formation is better understood, it seems wise to aim at early oxygenation and the removal of inspired material from the trachea and the main bronchi

Results with Gastric Oxygen

We have no experience of giving gastric oxygen alone to mature infants because we have hesitated to deny them the benefits of endotracheal oxygen

Since June 1952 gastric oxygen has been the routine treatment for apnœa in premature infants, and every infant so treated has become pink We therefore rely on gastric oxygen to give some oxygenation of the blood stream and to enable the babies' respiratory centres to recover During this time postural drainage and pharyngeal suction are practised. If the baby cannot subsequently expand its lungs in spite of making respiratory efforts it is treated by augmented respiration

Improvement in Colour in Spite of Prolonged Apnœa

Case 15 —Birth weight 2 lb 8 oz at 30 weeks. Lived $3^1/_4$ hr on gastric oxygen and became pink without making a single spontaneous respiration Necropsy showed cerebral hæmorrhage

Satisfactory Respiration following Gastric Oxygen

Case 16 —Birth weight 2 lb 10 oz. at 32 weeks. Cæsarean section for severe hæmorrhage from placenta prævia. No spontaneous respiration Given gastric oxygen and intramuscular nikethamide Started to gasp 10 minutes after delivery Was still mildly cyanosed $2^1/_2$ hr after birth but subsequently did well

Case 17 —Birth weight 2 lb 10 oz. at 32 weeks. Induction for pre-eclamptic toxæmia (exchange resins) No response to oxygen and rocking for 10 minutes Gastric oxygen given at 10 minutes Baby responded to passage of tube—breathed. Gastric oxygen discontinued in 3 minutes

Respiration Established—continuing Rib Recession

Case 18 —Birth weight 1 lb. 9 oz at 28 weeks No spontaneous respirations in spite of pharyngeal suction and oxygen by face mask. Given gastric oxygen at 5 minutes Became pink at 10 minutes Breathed regularly but showed rib recession Gastric tube removed at 5 hours Sudden apnœa at 25 hours Died

Discussion

It can be calculated from the Registrar General's returns for 1949 that 17% of deaths in the first four weeks were attributed to asphyxia A similar calculation made from the annual report for 1950 for the county of London gives a figure of 21 6% Both these figures are probably too high, for it is notoriously difficult to diagnose the cause of death of newborn babies on clinical evidence alone Where a careful post mortem study has been made, however, it is still found that asphyxia causes a large proportion of the neonatal deaths For example, Potter and Adair (1943) found that 18% of 284 neonatal deaths were due to asphyxia

Some workers who have used endotracheal intubation have published figures illustrating their results

Fletcher and Rogers (1951) had 66 neonatal deaths in 2531 deliveries, 23 of these were due to asphyxia (9 per 1000)

Cappe and Pallin (1951), in 16,766 deliveries in which endotracheal suction, followed if necessary by insufflation, was the treatment for asphyxia, had a neonatal mortality of only 13 8 per 1000

Russ (1946), who intubated all of a consecutive series of 317 babies born by cæsarean section, achieved an 18 per 1000 mortality among babies delivered by this means compared with 87 per 1000 for a control group of 137 "cæsarean" babies

In contrast to the findings cited above and summarised in table v, a study of the published annual reports of several large maternity hospitals, where the standard of obstetrical care is comparable to our own and where most of the infants that die are examined post mortem, shows that at these hospitals asphyxia contributes only a small proportion of the total of neonatal deaths

Conclusions

The routine of this hospital for the immediate resuscitation for asphyxia neonatorum is early aspiration, endotracheal insufflation for mature infants, and gastric oxygen for small premature infants Persistent atelectasis is treated by augmented respiration We believe that endotracheal intubation is safe in skilled hands, and that this method, combined with the other procedures described, should reduce postnatal deaths from uncomplicated asphyxia to a minimum

We cannot claim that our methods are superior to others We reaffirm, however, that it is only by having a well planned and efficiently practised technique of resuscitation in the labour room that the number of deaths from this cause can be reduced Deaths from postnatal asphyxia are to a large extent preventable

We wish to thank Prof J McClure Browne for his coöperation, and Prof A A Moncrieff for his help and enthusiasm, which encouraged us to write this article

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THERAPEUTIC TRIAL OF
THE SYNTHETIC HEPARIN ANALOGU
DEXTRAN SULPHATE

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THE naturally occurring anticoagulant, heparin, i sulphuric ester of a complex polysaccharide The h of the chemical identification of heparin, and a re of its biological activity and therapeutic app have been presented by Jorpes (1946) Bergstrom (1936) and Chargaff et al (1936) showed that the sul esters of other polysaccharides have a similar but w anticoagulant activity This led to a search for s thetic substitute for heparin The toxicity of the sul esters of starch, glycogen, chitin, and various polysaccharides was investigated by Astrup and (1946), who found them to be active anticoagulant unsuitable for clinical use because in compar dosage they produced in laboratory animals a ten to bleeding

Sulphuric esters were prepared from dextran various molecular weights by Gronwall et al (1945) reported that the toxicity of their compounds de as the molecular weight decreased, but they did produce a satisfactory therapeutic compound Recent in Birmingham, investigations have been made in wh the differences in the molecular weight of the r dextran and of the sulphur content of the final have been related to toxicity and biological activ (Walton 1951, Ricketts 1952a, Ricketts and W 1952, Walton 1952, 1953a and b)

In experiments on animals it was found that molecules of dextran sulphate must be of an o size to reduce their toxicity to a level comparable that of heparin, and that a certain threshold of su content must be exceeded to ensure satisfactory a coagulant activity Molecules of dextran sulphate dimensions above the optimum size formed insol precipitates with the plasma proteins and especially f fibrinogen (Walton 1952) This was found to be asso with agglutination of the formed elements of the b (Walton 1953a) and with storage of the material reticulo endothelial cells and with other undesir pathological changes (Walton 1953b) On the o hand, molecules which were much smaller than optimum size were ineffective in vivo—pre cause of very rapid passage out of the blood-stream icketts 1952b and unpublished observations)

Dextran-sulphate molecules of optimum size and lphur content though less potent, weight for weight an commercial heparin appeared to behave in a quali tively similar biological fashion and to show com rably low toxicity (Walton 1953b) When the optimum olecular characteristics of dextran sulphate from the andpoint of its possible use as a substitute for heparin d been defined, a batch was prepared in the laboratory icketts 1952a) in an amount sufficient to allow thorough ological screening and subsequent therapeutic trial on limited scale at Birmingham

Pilot Clinical Trial

METHODS

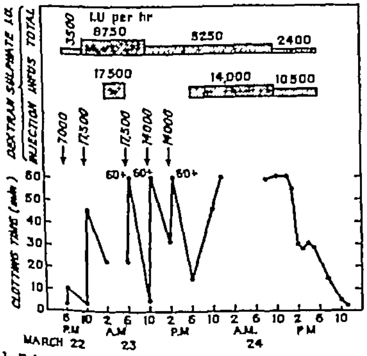
A 20% (*w/v*) solution of the material (batch I/3) in ysiological saline solution was sterilised by Seitz tration and tested to ensure sterility and freedom from rogens. The material was assayed against international ndard heparin by the method of Kuizenga et al (1943) d its potency expressed in heparin units. The solution ed contained 3000 units per ml

In the preliminary clinical trial at Birmingham no tempt was made to show clinical efficacy equal to or eater than that of heparin The limited objectives re (1) to show that dextran sulphate was an effective ticoagulant in man in vivo; (2) to establish, as far as ssible that its use was not attended by toxic effects her immediate or remote and (3) to obtain prelimi ry information about dose response relations. To fulfil e last of these aims dosage-levels were changed fre ently and the clotting time was measured two hourly the method of Dale and Laidlaw (1911–12) on pillary blood taken from the ear

The dextran-sulphate solution was administered intra nously either intermittently by repeated venepuncture se 1) or by continuous intravenous infusion in a solution 5% glucose in 0 45% saline solution (cases 1 2, and 3) uring therapy the following investigations were made total and differential estimation of plasma-proteins cluding fibrinogen) (2) full blood-count (including atelets) (3) erythrocyte sedimentation rate (E.S.R.) chemical and microscopical examination of the urine estimation of urinary excretion of dextran sulphate th toluidine-blue by the method of McIntosh (1941)

RESULTS

Case 1.—A man, aged 48, was knocked down by a falling ter On admission to the Birmingham Accident Hospital had flaccid paralysis of both legs, with anæsthesia below L1 Radiography showed a fracture-dislocation of the spine in the region T_{11} and T_{12} Open reduction was performed the same day Between the tenth and twelfth days a slight fever was noted and the right leg and thigh were seen to be swollen and discoloured The patient complained of a sudden pain in the right chest, which became worse with inspiration A diagnosis of venous thrombosis and pulmonary embolism was made



1—Dale and Laidlaw (1911–12) clotting-time response to dextran sulphate in case 1

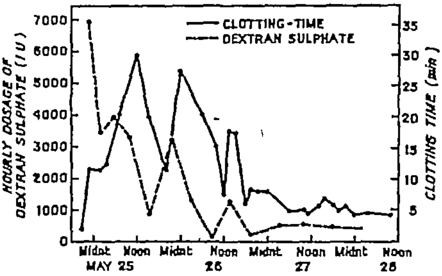


Fig 2—Dale and Laidlaw (1911–12) clotting-time response in case 2 to continuous infusion of dextran sulphate in saline solution by intravenous drip.

Anticoagulant therapy with dextran sulphate was initiated The dosage schedule of dextran sulphate and the clotting time response are shown in fig 1 After ten hours therapy the patient said that the pain in his chest had abated His temperature, pulse rate, and respiration rate were unaltered.

On the second day of treatment the method of administration was changed from intermittent injections to continuous infusion. The clotting time response altered from a succession of sharp peaks (the ' picket-fence ' curve of Duff et al 1951) to a smooth curve The clotting time could be kept reasonably steady at any desired level by appropriate adjustment of the drip-rate of the infusion

At the end of forty-eight hours the patient's colour and general condition were good, and no untoward effects had been produced by the dextran sulphate No alterations were observed in the levels of the platelets, white cells, and hæmoglobin or in the E.S.R. The plasma-protein levels were unaltered. Examination of the urine showed no abnormality Estimation of the dextran sulphate excreted in the urine (as material giving a metachromatic reaction with toluidine-blue) showed excretion of such material sporadically After forty eight hours the administration of dextran sulphate was discontinued. The clotting time was restored to its pre treatment level *in four and a half hours Anticoagulant therapy* was then resumed with heparin. The patient made an uneventful recovery and six months later was well and walking in callipers.

Case 2—A man aged 57 had had two previous attacks of thrombophlebitis involving first the left and then the right leg during the preceding year He was admitted to the Queen Elizabeth Hospital for investigation because of increasing dyspnœa and because a dense hilar shadow was seen when his chest was radiographed After five days in hospital he developed pain and swelling in his right leg with tenderness over the femoral vein in the groin and mid thigh A recurrence of thrombophlebitis was diagnosed.

Dextran sulphate was administered by continuous intravenous infusion for three and a half days The pain in the leg abated within eight hours, and the swelling had decreased by the third day of treatment The clotting time response is shown in fig 2. No untoward reaction was observed during the period of therapy and pathological investigations showed no deviation from the pre treatment values. During therapy the excretion of material giving a metachromatic reaction with toluidine-blue was noted in the urine

During dextran sulphate therapy the prothrombin time estimated by the one-stage method of Quick (1935) consistently showed a reduction to 30% or less. After three and a half days the treatment with dextran sulphate was discontinued. The clotting time was restored to normal in three and a half hours. Anticoagulant therapy was then resumed with Tromexan (3 3'-carboxymethylene bis-(4 hydroxycoumarin) ethyl ester) With physiotherapy and anticoagulants the condition in the right leg cleared to give a satisfactory result Six months later the patient was well and had had no further recurrence of thrombophlebitis

Case 3 —A man, aged 57, was knocked down by a motor-cycle, a week before admission On admission to Birmingham Accident Hospital no fracture was found on radiography, but there was gross swelling of the thigh, bruising of the right leg, and effusion into the right knee joint Six days later the swelling in the thigh was firm and indurated Tenderness extended along the saphenous vein as far as the pelvis A diagnosis of intramuscular hæmatoma with saphenous and femoral thrombosis was made It was considered that anticoagulant therapy might prevent extension of the latter, though the danger of possible renewal of bleeding from the torn veins in the thigh was recognised The patient's hæmoglobin was 60% of normal

Therapy with dextran sulphate was started by continuous infusion after three pints of blood had been transfused During the subsequent twenty four hours the patient's general condition improved He stated that the pain in his leg eased eight hours after the commencement of the infusion The tenderness over the femoral vein was less About thirty six hours after therapy began the patient complained of a sudden renewal of acute pain in the leg, with a feeling of tightness Bruising and discoloration of the skin on the lateral aspect of the leg (where none had previously been present) became apparent, suggesting renewal of bleeding from the site of injury The infusion of dextran sulphate was stopped Two pints of whole blood was transfused The clotting time was restored to normal in two hours, and there was no further swelling of the leg Ten days later the swelling appeared to be subsiding rapidly and the patient was up on crutches Thereafter, with the aid of massage and exercises, the patient's condition continued to improve Six months later the patient was well, with almost full movement of the limb

The results obtained in the first three cases were considered sufficiently encouraging to warrant further trial Material manufactured on a pilot commercial scale was supplied to three centres with considerable experience of anticoagulant therapy with heparin, for independent assessment

Extended Clinical Trials

MATERIAL

Two batches of dextran sulphate were prepared on a larger scale

These batches differed slightly in their method of production The first batch (no 5221) was produced by a method essentially similar to that used for the production of the material used in the preliminary clinical trial at Birmingham—i e, the material was made by sulphation of a dextran fraction considered to be of suitable molecular size Further experience of manufacture on this scale of production showed that this method did not ensure a constant uniformity of optimum dispersion of molecular size in successive batches A modification was therefore introduced into the method of preparation designed to ensure greater homogeneity of molecular size at the required level This modification consisted in fractionation of the final product, dextran sulphate, itself In the case of both batches the dextran sulphate, in the form of its sodium salt was dissolved in a buffered isotonic solution containing 0 72 % sodium chloride and 0 24 % sodium bicarbonate, sealed in ampoules, and sterilised by autoclaving The ampouled material was tested for sterility, pyrogenicity, and freedom from toxicity in vivo in a manner similar to that previously described (Walton 1953b) Both batches satisfied these requirements

The anticoagulant activity of the material was again assayed against a sample of international standard heparin The concentration of dextran sulphate was adjusted so that the final solution used contained either 900 or 1000 units per ml The characteristics of the two batches are as follows

Manufacturers' batch no	5221	52DSO39
Dextran sulphate (g per 100 ml)	5 7	8 15
Sulphur (g per 100 ml)	1 01	1 427
Intrinsic viscosity (dl per g)	0 03	0 03
Potency (heparin units per ml)	900	1000

It will be seen that, although both products showed the same intrinsic viscosity, indicating the same average molecular weight, they differed slightly in sul content and in activity

METHODS

In the extended clinical trials attention was ma directed to the following points

(1) The dose response relations were further investiga The technique of intermittent intravenous injections was almost exclusively since this is the method most used for heparin therapy

(2) Direct comparisons were made of the height duration of response to equipotent doses of heparin dextran sulphate in suitable cases

(3) A preliminary indication was looked for of the of individual variation of response to a given dose of sulphate

(4) Further confirmation of the lack of toxic effects sought

It is common clinical experience that, in cases thrombosis, heparin therapy is often attended by relief of pain and improvement in the general condition It has been suggested that this may be a vasodilator effect either generalised or localised to affected part Some preliminary observations were made, therefore, in selected cases, on changes in temperature after treatment with dextran sul Incidental observations were made to confirm the that dextran sulphate, like heparin, interfered with performance of the "prothrombin"-time test as w affecting the clotting-time Preliminary obser were made on the urinary excretion of dextran

CLINICAL TRIAL AT POSTGRADUATE MEDICAL SCHOOL LONDON

Batch 5221 containing 900 international units (I U) ml was used for this trial The work consisted in a istering (1) nine single intravenous injections of dosages to observe the effect on the clotting (2) repeated four-hourly intravenous injections (th the diaphragm of an indwelling Gordh needle) to patients to determine its efficiency as a thera agent, and (3) in one patient dextran sulphate compared with heparin on the same dosage

With Quick's modification (Quick et al 1949) of Lee and White (1913) technique, in which the clotting time is 5–10 minutes, adequate dosage regarded as that which prolonged the clotting about three times the normal when estimated an after injection

RESULTS

Single injections—Cases 4, 5, and 6 received venous i tions of 4500, 6750 I U dextran phate tively three occasions Clotting t were es ted before every h hour after each dose four hours response in three cases similar (fi All the clotting ti were normal After do

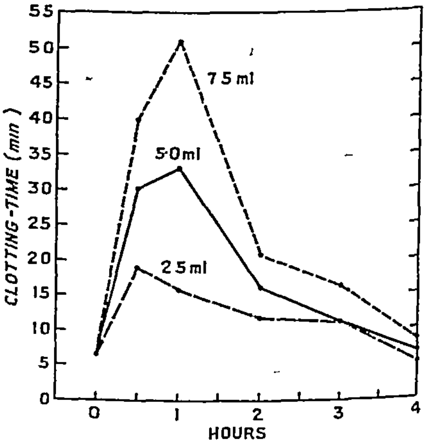


Fig 3—Lee and White (1913) clotting time response to single intravenous injections of dextran sulphate (1 ml = 900 I U) The curves show the means of the responses to different dosages in three normal people.

TABLE I—RESULTS OF CLINICAL TRIAL AT POSTGRADUATE MEDICAL SCHOOL OF LONDON

Diagnosis	Age (yr)	Initial clotting time (min.)	Drug and dosage (I U 4-hrly)	Clotting time (min.) after injection				Change in dosage (I.U 4 hrly)	Clotting time (min)			
				Day 1		Day 2			Day 3		Day 4	
				1 hr	4 hr	1 hr	4 hr		1 hr	4 hr	1 hr	4 hr
Popliteal thrombosis	75	9	Dextran sulphate 4500	20	13	51	17	None	60	19	92	25
Mitral valvulotomy venous thrombosis (calf)	35	6	Dextran sulphate 2700	12	8	14	8	Dextran sulphate 4500	15	10		
Myocardial infarction	70	8	Heparin 5000	27	8	32	7	Dextran sulphate 4500	32	18	72	18

0 4500 and 6750 I U of dextran sulphate, the longest tting times were recorded either half an hour or an r after injection, the mean figures being 17 28 and minutes respectively Four hours after injection the tting time in response to 2250 I U had returned to mal but was slightly prolonged in response to the her doses.

epeated injections—Treatment was given for periods to four days Case 4 received 4500 I U four hourly for r days, and case 5 received 2700 I U four hourly, reasing after two days to 4500 I.U four hourly for a ther day Case 6 received injections of 5000 I U of arin four hourly for two days After the clotting time l returned to normal 4500 I U of dextran sulphate given four hourly for a further two days In all three es the clotting times were estimated before therapy gan and subsequently twice daily, an hour and four rs after an injection The results are shown in table I se 4 receiving 4500 I.U four hourly showed a progres e increase in clotting time, the one hour clotting time ng 20 minutes on the first, and more than 90 minutes the fourth day of treatment. This additive effect ggested that at this dosage injections were being en too frequently—i.e. that at equipotent dosage duration of effect of dextran sulphate was greater n that of heparin This was borne out by the response case 5 in whom on a dosage of 2700 I U of dextran phate four hourly the clotting time was back to rmal after four hours but on a dosage of 4500 I U s still increased after four hours Direct comparison heparin and dextran sulphate in case 6 showed that ereas 5000 I.U of heparin four hourly produced mparable one-hour and four hour responses on con utive days, 4500 I U of dextran sulphate four hourly duced a progressive increase in the clotting time ponses at these intervals after injection

Side-effects—In case 4 receiving dextran sulphate 4500 I U four hourly a spontaneous bruise 4 cm in diameter appeared on the left forearm on the third day when the clotting time an hour after injection was 60 minutes. Apart from this no toxic or hæmorrhagic effects were seen

Investigations—Daily microscopy of the urine showed no red blood cells in any of the patients treated The E.S R. did not vary with changes in the clotting time Measurements of the skin temperature of the limbs after intravenous injection of dextran sulphate showed no significant rise of temperature

CLINICAL TRIAL AT GLASGOW ROYAL INFIRMARY

Batch 52DS039 containing 1000 I U per ml was used in this trial. Single intravenous injections were given to three volunteers and to a patient with coronary thrombosis (cases 7–10) Another volunteer (case 11) was given 5000 I U of the material intramuscularly a dose which was not considered to be of great practical value but was limited because of the relatively dilute solution available In cases 7 and 9 the effects of two similar intravenous doses given at intervals of seven to nine days were compared, and in case 10 the effects of equipotent doses of heparin and dextran sulphate were compared. The responses obtained are shown in table II It can be seen that after intravenous doses of 5000 I U the clotting time had not reverted quite to normal at the end of four hours (cases 8 and 10 (i)) The magnitude of the effect was greater with 10 000 I U intravenously (cases 7 and 9) but its duration was not obviously lengthened In case 10 the anticoagulant effect of dextran sulphate lasted longer than that of heparin The intramuscular injection of 5000 I U did not produce pain at the site of injection but produced only a slight lengthening of the clotting time. No toxic or hæmorrhagic effects were observed in the

TABLE II—RESULTS OF CLINICAL TRIAL AT GLASGOW ROYAL INFIRMARY

	Sex	Age (yr)	Diagnosis	Drug and dose (I U)	Route	Lee-White clotting time (min.)						Comment
						Before	Hours after					
							½	1	2	3	4	
	M	10	Previously anæmic	(i) Dextran sulphate 10 000	I V	8	55	10	29	17½	14	No side-effects
				(ii) Dextran sulphate 10 000	I V	9	23	17	13	15	1[illegible]	2nd injection [illegible] days after first
8	F	52	Coronary thrombosis	Dextran sulphate 5000	I V	7	21	27		14	17	Patient died on day following injection; detailed case-history in text
9	F	62	Coronary insufficiency	(i) Dextran sulphate 10 000	I V	9½	65	30	35	33	25	Two injections 9 days apart gave similar curves no side-effects
				(ii) Dextran sulphate 10,000	I V	9	70	1[illegible]	[illegible]	2	12	
10	F	45	Rheumatoid arthritis	(i) Dextran sulphate 5000	I V	12	[illegible]	50[illegible]	[illegible]0	[illegible]2	10½	Two injections one day apart; no side effects no vasodilator effect
				(ii) Heparin 5000	I V	9½	11½	31	[illegible]0	11	9½	
11	M	54	Coronary insufficiency	Dextran sulphate 5000	I.M*	8	11	10	11½		11	No pain at site of injection no side-effects

* Intramuscular dose limited by volume to be administered.

TABLE III—RESULTS OF CLINICAL TRIAL, DEPARTMENT OF SURGERY, UNIVERSITY OF EDINBURGH

Case no	Sex	Age (yr)	Diagnosis	Dextran sulphate Dose (I U)	Dextran sulphate Days	Other therapy	Days	Result	Complicati
12	M	76	Deep venous thrombosis (femoral and calf veins)	5000 daily	6	Heparin	14	Good	None
13	M	40	Deep venous thrombosis (femoral and calf veins)	5000 daily	5	Heparin Elastic stocking	14	Good	None
14	M	44	Deep venous thrombosis (calf veins)	5000 b d 5000 daily	2 3	Heparin 10,000 I U b d	6–21	Good	None
15	F	64	Deep venous thrombosis (calf), pulmonary embolus	5000 b d	5	Heparin 10,000 I U b d	12	Good	None
16	M	60	Arteriosclerosis obliterans, arterial thrombosis of left leg	5000 daily	17	Reflex heating	17	Satisfactory	Vomited on day, otherwi
17	M	64	Arteriosclerosis obliterans gangrene of right 4th and 5th toes	5000 daily	13	Buerger's exercises	13	Ulcers healing, claudication unaffected	Died, [illegible] hæmorrhage on day (see text)
18	M	43	Mesenteric and popliteal embolism	5000 b d 5000 daily	1 9	Heparin 10 000 I U daily	60	No return of pulses at $3\frac{1}{2}$ mos	None
19	F	64	Deep venous thrombosis	5000 (single dose)					None
20	M	52	Intermittent claudication	5000 (single dose)					None

cases in this series One patient died of extensive myocardial infarction on the day following the administration of dextran sulphate The case-history was as follows

Case 8—A woman, aged 52, was admitted to Glasgow Royal Infirmary with nine months' history of attacks of anginal pain relieved by rest and of increasing breathlessness on exertion A severe attack of "tearing" pain in the retrosternal region radiating towards the neck, with much weakness and nausea had come on nine days earlier and again on the day of admission. Coronary thrombosis with myocardial infarction was diagnosed Dextran sulphate 5000 I U was given intravenously at 2 35 P M and again at 12 45 A M on Jan 13, 1953 'Dindevan' (phenylindanedione) 150 mg was given at 12 45 A M. on Jan 13 Morphine sulphate gr $\frac{1}{4}$ was given at 12 25 P M, 4 50 P.M, and 10 45 P M on Jan 12 and at 1 20 P M on Jan 13 The patient became fairly comfortable after the initial administration of morphine and was pain free by 9 00 A M the following day By midday it was noted that the patient was becoming very shocked The pulse was very irregular, the systolic blood pressure was 80 mm Hg and the diastolic unobtainable In the heart, coupling and numerous extrasystoles were observed The patient became breathless, distressed, and restless, and died at 1 00 P.M

Post mortem the only significant findings were in the heart, the other thoracic and the abdominal organs being apparently normal The heart (420 g) was enlarged owing to dilatation of both ventricles An extensive area of recent infarction involved the lower half of the interventricular septum Nodular patches of atheroma were present in the coronary vessels, and the descending branch of the left coronary artery contained a thrombus adherent to the wall and filling the lumen from its origin for a distance of two inches

Microscopy of the liver, spleen, myocardium, adrenals, and kidneys showed no evidence of pathological change attributable to the dextran sulphate Sections stained toluidine blue showed no evidence of storage of giving a metachromatic reaction in reticulo-endothelial

CLINICAL TRIAL IN DEPARTMENT OF SURGERY, UNIV OF EDINBURGH

Batch 52DSO39 containing 1000 I U per ml was for this trial It was administered to seven (cases 12–18) by intermittent intravenous injections periods varying from two to seventeen days observations were also made in two other patients 19 and 20) Cases 16 and 17 were treated as being kept under observation for three or four hours each injection to allow the maximum effect of the to wear off

Results

The clinical results of therapy are shown in table from which it can be seen that they were good in cases of deep venous thrombosis and fairly good in case of multiple arterial emboli (mesenteric and fe Two patients with arteriosclerosis obliterans and of recent spread of thrombosis in one leg (cases 16 17) were treated with single intravenous in dextran sulphate 5000 I U for seventeen and days respectively Their claudication distances did alter during this time, but both patients spontane mentioned a subjective feeling of heat in one or feet, and in one patient (case 17) small ischæmic on the toes showed signs of healing by the tenth However, this patient, who had been treated as outpatient, died suddenly on the fourteenth day

TABLE IV—EFFECT OF DEXTRAN SULPHATE ON CLOTTING TIME AND ONE-STAGE "PROTHROMBIN" TIME

Case no	Age (yr)	Lee White clotting time (min.) at 37°C							Prothrombin time (Quick's one-stage) (sec.)						
		Before	Hours after dextran sulphate 5000 I.U I V						Control time	Hours after dextran sulphate 5000 I.U I V					
			$\frac{1}{2}$	1	2	3	5	7		$\frac{1}{2}$	1	2	3	5	
12	76	13	100 +			28	25	15	15 3	20 3			21 7	20 9	16
13	40	17*		90		47	22		17 4		20 2		20	19	
14	44	18*		85		24	26	19	16 8		23 4		22 9	20 3	19
15	64	10		25	28	18	12								
16	60	8	120 +	40	42	30	17		15 5	24 4	22 7	20 8	19	15·5	
18	52	7		49	57	43			17 3		20 7	21 3	20 1		
19	64	14			90 +		26		15 3			22 7		20 7	

*Cases 13 and 14 showed unusually protracted responses to dextran sulphate The administration of 5000 I U twenty four hours was thought to be responsible for the high base line clotting times shown in either case enty hours after his last injection, with signs of ebral hæmorrhage. Necropsy was not performed and further details could be obtained from his doctor In lition to the signs of severe obliterative arterial disease the legs this patient had electrocardiographic changes licating myocardial ischæmia, and his blood pressure s 225/105 mm. Hg This patient was, in any case a sible candidate for a cerebral vascular accident and re was nothing to suggest that the incident took place en dextran sulphate was exerting an important icoagulant effect

Effects on clotting-time —The effects on the clotting e in seven patients and on the one stage prothrombin e (Quick 1935) in six patients for periods up to seven urs after the injection of dextran sulphate 5000 I.U shown in table IV It can be seen that although the ial response resembled that which might be expected m an equipotent dose of heparin the effect lasted ger A satisfactory clinical response was obtained in the cases treated with 5000 I U twice daily or in some es once daily Case 13 showed a much greater response n did the other patients to dextran sulphate his tting time was 21 minutes twelve hours after the injec- n of dextran sulphate 5000 I U on one day and on other day 17 5 minutes fifteen hours after a similar e. Case 14 showed a similar though less well marked ponse to the material These two cases are discussed ow

ther observations —Three patients remarked on a jective feeling of warmth which sometimes lasted o hours after an injection. Skin temperature record s were made in five patients Four of the five patients wed increases of 0 8°–5 5 C in skin temperatures, and effect was observed repeatedly in two patients The ximum effect did not occur until half to one hour r the injection The E.S.R did not vary significantly h changes in the clotting time but an occasional ease was noted.

EXCRETION OF DEXTRAN SULPHATE

aterial giving a metachromatic reaction with tolu e blue was found to be excreted in the urine during rapy with dextran sulphate in cases 1 and 2 This ervation was confirmed in cases 13 14 and 15 liminary quantitative studies showed that (1) hough the urinary level of this material decreased onentially after a single intravenous dose the total ount excreted appeared to vary with the volume of e secreted and to be increased by even a slight resis (2) considerable variation was found in the al daily excretion even in the same person on constant age on different days and (3) no correlation was onstrable between urinary excretion and sensitivity response of the clotting time For instance case 14 whom dextran sulphate produced an unusually tracted prolongation of the clotting time showed a ater daily excretion on the same dosage, than case 15 o showed a normal clotting time response This gested that increased sensitivity of response was not to failure to excrete dextran sulphate but possibly a slower rate of its inactivation in the blood-stream ther studies of this aspect are in progress In par lar, experiments with dextran sulphate of similar lecular composition but labelled with radioactive phur (S^{35}) are now being made to obtain a clearer ture of the metabolism and excretion of dextran phate

Discussion

From a consideration of the response in the twenty r people to whom dextran sulphate was administered ting the various clinical trials reported above it is ar that dextran sulphate serves as an effective anti ulant in clinical practice The clotting time response intravenous injection resembled that to equipotent doses of heparin in that intermittent dosage produced a picket fence curve and continuous infusion gave a smooth curve adjustable to any given level by appropriate adjustment of the rate of administration

The most noticeable difference was that of duration of effect Heparin 5000 I U administered intravenously prolongs the clotting time for 2 or 3 hours (Estes and Allen 1950 Duff et al 1951 Brown and Douglas 1952) The equivalent dosage of dextran sulphate produced an effect for five to seven hours. Thus when doses of dextran sulphate of this order were given by intermittent four hourly injections an additive response was obtained On the other hand, a constant clotting time response and satisfactory clinical results were obtained with a dosage of 5000 I U twice daily The intravenous administration of dextran sulphate produced an unusually prolonged effect in two patients (cases 13 and 14) This does not appear to have been due to failure to excrete the material effectively (see above) In these patients single daily injections were judged to be sufficient to secure the desired clinical effect Possibly these patients were hyper reactors ' to dextran sulphate Considerable differences in sensitivity of response to heparin have been reported in animals (Jaques and Ricker 1949) and in man (De Takats 1943 Duff et al 1951) De Takats reported that of 87 patients subjected to a heparin tolerance test 8 were found to be hyper reactors, 47 reacted normally and 32 were 'hypo reactors. The present series of patients treated with dextran sulphate is too small to yield similar information about the distribution of sensitivity of response to the synthetic analogue. From preliminary unpublished observations it seems likely that sensitivity of response to dextran sulphate may parallel that to heparin, but further information on this point also will have to await more extensive clinical experience

Since it is common practice to use heparin to cover the period of delayed effect encountered with the coumarin derivatives, it is of interest that dextran sulphate like heparin interfered with the 'prothrombin' time estimated by Quick's one-stage method This suggested the advisability, where dextran sulphate is used before coumarin therapy of taking a blood sample for the control "prothrombin' time before the administration of either type of drug

STANDARDISATION OF DEXTRAN SULPHATE

The material used in the present clinical trials was assayed and labelled in terms of heparin units This was an interim measure for the convenience of clinicians accustomed to heparin dosage in these terms and to facilitate the comparison of equipotent doses of the two anticoagulants. It was fully realised that comparison of potency on the basis of parity of in vitro activity might be regarded as unsatisfactory but it was felt to be necessary to provide a known and familiar yardstick for the preliminary work with dextran sulphate In view of the observed difference in duration of effect a sample of dextran sulphate has been submitted to the World Health Organisation Committee on International Biological Standards with a proposal that a provisional standard should be established for dextran sulphate itself

DOSAGE

From the evidence so far available it is concluded that dextran sulphate as at present standardised will produce a satisfactory clinical response in most cases when given intermittently at a dosage of 5000 I U six hourly or when given by continuous infusion at a dosage of 500–750 I U hourly

SIDE EFFECTS

In the cases so far treated no toxic side-effects have been observed Hæmorrhagic complications were noted in two cases a spontaneous bruise was observed in case 4, and recurrence of bleeding occurred in a recently traumatised limb in case 3 From the latter experience, it is apparent that dextran sulphate is no safer than any other anticoagulant for use where there has been recent bleeding On the other hand, cessation of dextran-sulphate therapy was followed by restoration of the clotting-time to normal in four or five hours, and this restoration was accelerated in emergency, as in case 3, by blood-transfusion In the present series no occasion arose for still more rapid counteraction of dextran sulphate, but it had been shown previously that the anticoagulant action of dextran sulphate, like that of heparin, is immediately neutralised by suitable amounts of protamine (Walton 1951)

Two patients died during the course of therapy In neither case was there any evidence that death was caused or accelerated by changes directly referable to the anticoagulant

The rate and magnitude of the skin temperature changes after intravenous injection of dextran sulphate were such as to make them of doubtful significance compared with the response usually obtained with drugs such as tolazoline hydrochloride ('Priscol'), which are thought to produce a vasodilator effect by direct blockage of the autonomic innervation to peripheral vessels and exert considerably quicker and more pronounced effects The slow and relatively feeble effect with dextran sulphate suggests that if there is any action at all it must be mediated by a more indirect mechanism It has been shown that intravascular blood clotting is accompanied by the release of a vasoconstrictor substance, sometimes described as "serotonin" (Janeway et al 1918, Hirose 1918, Zucker 1944, Rapport et al 1949), but that this substance is not released in heparinised blood Possibly the arrest of intravascular clotting, which may be presumed to take place during the treatment of thrombophlebitis with heparin or with dextran sulphate, may inhibit further production of such a vasoconstrictor substance and allow restoration of normal vascular tone Further experimental investigation of this aspect of these drugs is needed to support this hypothesis

Apart from its qualitatively similar activity to that of heparin as an anticoagulant, it has been reported that dextran sulphate also reproduces the behaviour of heparin in respect of other biological systems Its similarity of action in clearing the turbidity of lipid-laden plasma in vivo has been described by Brown (1952a b, and c) In addition it has been reported to inhibit the action of complement (Lambert and Richley 1952), to prevent the heat-coagulation of albumin (Hamer 1953), to act as an anti-hyaluronidase in high concentrations (C R Ricketts and M Hall, personal communication), and to prevent the release of histamine like substances from rabbit plasma in vitro (Haining 1953) The use of dextran sulphate as an anticoagulant for the collection of blood samples from cardiac catheters and indwelling arterial needles has been described by Wade, Bishop, Cummings, and Donald (1953) Other in vitro uses have been reported by Hall and Ricketts (1952)

COMPARISON OF DEXTRAN SULPHATE WITH EXISTING ANTICOAGULANTS

Until recently the choice of drugs for anticoagulant therapy has lain between heparin and one or other of the coumarin derivatives Heparin, though in many ways an ideal anticoagulant in allowing considerable latitude of dosage with safety, has certain disadvantages (1) it necessitates frequent parenteral administration, and (2) since it is derived from animal tissues, it is difficult and expensive to extract and purify, it gives rise occasionally to sensitisation reactions, probably from the presence of protein impurities, and when derived from different sources it seems to vary in chemical composition a physical characteristics (Jorpes and Gardell 1948)

Recently the therapeutic trials of three "heparin" preparations have been reported 'Paritol' (a sulp ester of polymannuronic acid) though an effective a coagulant, produced some undesirable reactions, the severe being a generalised vasomotor collapse (Seifter a Begany 1948, Sorenson et al 1949, Sorenson and Wr 1950) 'Thrombocid' and 'Treburon,' sulphuric e of other polysaccharides, have been reported to prod severe diarrhœa and late alopecia (May 1951, Field et 1953) During the present investigation of dext sulphate no similar toxic effects have been observed.

It appears from our present results that de sulphate resembles heparin in being comparably safe non toxic, in being quick-acting, in losing its e rapidly on withdrawal, and in its capacity for neutra tion in emergency It must also be administered pa terally, but its somewhat greater duration of antico lant effect allows its administration at longer inter The control of therapy requires no more elab investigation than estimation of the clotting time be each injection The relative ease of its manufac should allow cheaper production Since it is synthe from purified protein free material (dextran) it is unlikely to give rise to protein sensitisation react and it can be produced to specified chemical and p cal characteristics Its qualitatively similar effect biological systems, other than the clotting mechan which are influenced by heparin makes it a useful exp mental tool for the investigation of these phenom

Summary

Clinical experience of twenty cases in which dext sulphate was administered in various dosages and various periods, from a single injection to contin therapy for seventeen days, suggests that dextr phate is an effective anticoagulant producing a re qualitatively resembling that of heparin but la somewhat longer No serious side effects have observed

We wish to express our indebtedness to Prof J R S and Dr J P Bull for their interest and helpful crit during all stages of this investigation, to the Medical R Council Blood Transfusion Committee for help in the co of these trials, to Prof Melville Arnott and Mr J Clarke for their coöperation in allowing us access to the for the preliminary clinical trial at Birmingham, to Sir Learmonth, Dr J F Goodwin, and Prof L J Davis fo supervision of, and interest in, the cases treated in Edin London, and Glasgow respectively, and to Prof. G Montgomery for permission to summarise the necropsy on case 8 and for access to the blocks and sections of necropsy material In particular, our thanks are d Messrs. Dextran for the gift of dextran sulphate prepared to our specification for the extended clinical and to their technical staff for enthusiastic coöperation meeting our requirements. The dextran sulphate used in trials described above is the subject of Patent Ap no 695,787 and other applications which have been a to the National Research Development Corporation, 1, T Street, London, W 1

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HYPOTHERMIA

AN EXPERIMENTAL STUDY OF SURFACE COOLING

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One barrier to further advances in cardiac and cerebral urgery is the difficulty of maintaining an adequate w of oxygenated blood to the vital organs during mplex surgical operations Hypothermia by reducing e body temperature and consequently the body etabolism is one method of attaining this end It has en used on a limited scale in medicine and surgery for any years; in the Napoleonic era local cooling of the sues was successfully used for amputations during the treat from Moscow More recently, general body cooling s been suggested as a method of treatment of cancer mith and Fay 1940) and for use in surgery in man igelow et al. 1950 Juvenelle et al 1952a Delorme 52 Cookson et al 1952)

The method most widely adopted for reducing the dy temperature is cooling the environment of the æsthetised patient. Delorme (1952) has suggested that oling the blood by an artificial arteriovenous anasto- osis may have certain advantages. The creation of an teriovenous fistula alone, however causes profound ysiological changes (Holman 1937) and entails an lditional operation with its concomitant risks. We have ed this method as well as cooling of the pleural and peritoneal cavities with either cold water or a cooling coil. In each case the body temperature was reduced satisfactorily but of all the methods studied surface cooling appeared to be the simplest and safest technique and for this reason an investigation was undertaken to reassess the possible dangers before its application to surgery in man

Method

30 unselected mongrel dogs weighing 8–15 kg were used. Each dog was premedicated with promethazine hydrochloride ('Phenergan') 5 mg per kg of body weight subcutaneously Anæsthesia was induced with intravenous thiopentone sodium 0·015 g per kg of body weight followed immediately by succinylcholine chloride 5 µg per kg of body weight. The trachea was intubated, a cuffed tube being used, and anæsthesia was maintained with oxygen and ether in a closed-circuit apparatus with carbon dioxide absorption

When the dog had been anæsthetised control readings of body temperature, pulse rate blood pressure, electrocardiogram and oxygen consumption were taken The dog (unshaven) was next immersed in a bath of water at about 18–20 C After a few minutes crushed ice was added so that the temperature of the water rapidly fell to 2–6°C 20 dogs (series I) were cooled in this manner until their rectal temperature had fallen to 24°C when they were stabilised at 22–24°C for at least thirty minutes before being rewarmed. 10 dogs (series II) were cooled in an identical manner to 28–26°C for a similar period and then rewarmed. In both series the body temperature continued to fall a further two or three degrees after removal of the iced water from the bath

Rewarming was done by raising the temperature of the water in the bath to 42°C With the onset of shivering and returning consciousness the dog was removed from the bath dried, and placed in a warm recovery room

The body temperature was measured with thermocouples, one placed high up in the rectum or in the sigmoid colon and another inserted through the jugular vein into the right auricle In later experiments the rectal temperature alone was recorded, because the difference between the two readings was never more than ±1°C. All the readings were periodically checked against a standardised centigrade thermometer throughout each study

Blood pressure was measured with a mercury manometer connected to a cannula in the right femoral artery

The electrocardiogram lead II was continuously displayed on an oscilloscope throughout each study

Oxygen consumption was determined with a Benedict-Roth spirometer filled with the anæsthetic mixture of oxygen and ether

Defibrillation, when used, was preceded by cardiac massage and the intracardiac injection of 0 5 ml 1 : 1000 adrenaline sulphate when the fibrillation was not vigorous. The voltage used was 150–300V with a duration of 0 2 millisec. (McMillan et al 1952)

Results

SERIES I

The mean values of the body temperature blood pressure pulse rate, respiratory rate and oxygen consumption of 20 dogs cooled to 24–22°C are shown plotted against time in the accompanying figure

Blood-pressure showed a slight initial rise at the start of cooling but then fell gradually with the body temperature to about 29–26°C when the fall in blood pressure became more rapid in relation to the body temperature The average mean blood pressure in the anæsthetised dog at normal body temperature was 110 mm Hg falling to 48 mm Hg at 22°C—a reduction of 56%

Pulse rate fell gradually in unison with the body temperature The mean control value at normal body

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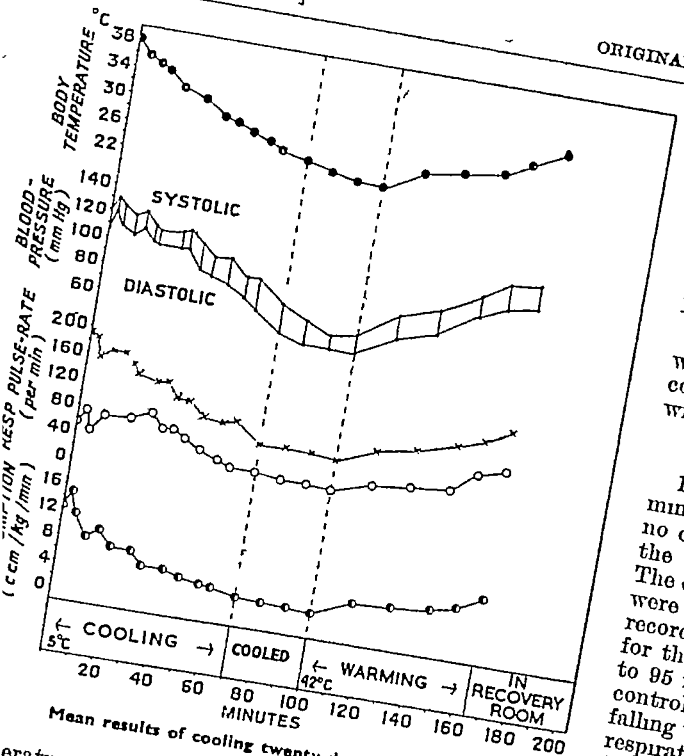

Mean results of cooling twenty dogs to 24–22°C

temperature was 192 per min , falling to 58 per min at 22°C—a reduction of 70%

Respiratory rate increased when the dog was first immersed but afterwards gradually diminished as the body-temperature fell, finally ceasing at various temperatures depending largely on the depth of anæsthesia 7 dogs (35%) were still breathing at 23–21°C when rewarming was started, whereas 6 (30%) stopped breathing at 27–26°C, and the remainder (35%) at 24–19°C The mean respiratory rate of the anæsthetised dogs at normal -body-temperature was 56 per min , falling to 8 per min at 22°C—a reduction of 86%

Oxygen consumption was progressively reduced as the body-temperature fell The extent of the fall above 28°C depended largely on the depth of anæsthesia , below this temperature a strikingly uniform reduction was noted The mean control value at 38°C was 12 6 c cm per kg of body-weight per min , falling to 5 2 c cm per kg body-weight per min at 28°C, and to 2 0 c cm per kg of body-weight per min at 22°C—a reduction of 84%

Shivering was observed in 3 dogs during cooling It was abolished by increasing the depth of anæsthesia in each case

Cardiac arrhythmias were observed in 14 dogs (70%) at 24°C or less, whereas the remainder (30%) maintained a normal rhythm at 22–19°C The electrocardiographic changes most often observed were prolongation of the P–R interval and Q R S complex, flattening and deep inversion of the T waves, and depression of the S–T segment

Rate of Cooling —The average time taken to reach 24°C from normal body-temperature was 70 minutes

Mortality and Morbidity —There were 5 deaths in this series, the other dogs showing no ill effects from the cooling

Dog no	*Cause of death*	*Body-temp (°C)*	*Time of death*
1	Pulmonary collapse	38 2	48 hr after study
2	Ventricular fibrillation	22 5	93 min. from start of cooling
3	Ventricular fibrillation	22 0	80 min
4	Ventricular fibrillation	22 0	140 min
5	Pulmonary œdema	38 0	8 hr after study

Each case of spontaneous ventricular fibrillation was preceded by a variable period of cardiac arrhythmias All [illegible]mpts at resuscitation failed

Dog 1 made an apparently uneventful recovery V it was eating well in the morning, but it became progr more drowsy as the day advanced and finally died fort hours after the study Necropsy showed gross collap both lungs, only the right lower lobe and part of the left lobe being aerated

Dog 5 made an uneventful return to normal tempera Six hours after the study it was walking around and wag its tail Two hours later, however, it was found de Necropsy showed severe pulmonary œdema

All these 5 deaths took place in adult dogs 4 pupp which were unaffected by this study were subsequent cooled to body-temperatures of 16°, 14°, 11°, and 10 without developing ventricular fibrillation

SERIES II

10 dogs were cooled to 28–26°C for at least th minutes and then rewarmed None of them died, a no cardiac irregularities were observed in this series, the dogs making a complete and uneventful recov The changes in pulse rate, blood pressure, and respira were similar in every respect, except degree, to th recorded in series I The average mean control val for the blood pressure at 38°C was 131 mm Hg, fall to 95 mm Hg at 28°C—a reduction of 27% The mea control value for the pulse rate at 38°C was 197 per m falling to 110 per min at 28°C—a reduction of 44% Th respiratory rate was the same at 38°C and 28°C, thou there was an initial rise at the start of cooling Th average time taken to reach 28°C was 44 min.

Discussion

This study represents a control series designed to sh some of the physiological changes that take place dur the reduction of body temperature by surface coo without any surgical intervention The results indic that surface cooling offers a simple and safe method reducing the body-temperature, provided the rec temperature does not fall below 26°C Below th temperatures cardiac arrhythmias become the rule a more rarely, proceed to ventricular fibrillation. from this, a lower body-temperature in dogs is f by an incidence of pulmonary complications which easily explicable

The method of premedication and anæsthesia us this study was chosen because it was most closely to that used in clinical surgery in man For this re the use of drugs was strictly limited The advantag the anti histamine drugs over the more conventi methods of premedication was not shown, but the of large doses of barbiturates and other respirat depressant drugs is contra indicated because the red metabolism leads to a more prolonged action, and th fore a delayed recovery, as had been shown in prev studies

Inhalational anæsthesia has the advantage th depth of anæsthesia can be controlled to abolish shi and yet allow the rapid return of consciousne rewarming It is believed that shivering during co may have serious consequences in patients with ca disease The use of the muscle relaxants obviates risk of shivering and at the same time allows a l level of anæsthesia, and it has been found that neo mine was an effective antidote to a competitive inhib block at 28°C in both man (1 case) and animals.

The use of carbon dioxide absorption under condit of hypothermia may be criticised on the grounds washing out carbon dioxide increases the effect of low temperature in shifting the oxygen dissociation c of blood to the left, thereby hindering the liberation oxygen to the tissues (Brown and Hill 1922, Pe 1951) It is unlikely that there was an excessive wash of carbon dioxide in these dogs, since assisted respir was not given, but this effect may be important in under controlled respiration

The absence of respiratory activity in some dogs at ·C and below depended largely on the depth of anæs esia but in all the cases respiration had ceased at °C At 30–28°C the dogs required only light anæs esia to prevent shivering and at about the same mperature the value for oxygen consumption became markably consistent from dog to dog On rewarming ontaneous respiration began again at 24–28°C

There is no doubt that the chief barrier to profound ypothermia is the risk of spontaneous ventricular brillation The cause of this at these low temperatures emains unknown, and some method of preventing it ust be found before cardiotomy can be done with afety under hypothermia Anoxic anoxia cannot be a ontributory cause, for full arterial oxygen saturation is aintained—indeed an additional amount of oxygen is ssolved in the plasma Also it has been shown that oronary-sinus blood is normally desaturated, suggesting at the heart muscle can still take up oxygen However ing et al (1949) point out that heart muscle under sual conditions at normal temperatures extracts con derably more oxygen from the blood than do other ssues, and they show that increased demand is met by increased perfusion rather than further arterial aturation. In this context may be cited the experi ents of Lange et al (1949) who subjected hypothermic bbits to an oxygen pressure of five atmospheres and so doing restored the electrocardiogram to normal milarly acidification of the blood temporarily led to e same result. The combination of hypotension low rdiac output, and decreased dissociation of oxygen ay well account for sufficient cardiac anoxia to induce rhythmias. A further suggestion which might explain e increased "irritability" is that it is due to a direct fect of cold on the pacemaker and conducting tissue uvenelle et al 1952b)

The finding that ventricular fibrillation at 22 C and low was irreversible must be emphasised Other orkers' experience, however confirms our own finding at it is reversible at higher temperatures (B A Cookson d D Ross, personal communications)

It may come to be regarded as axiomatic that the unger the dog the better it withstands the cold. In is respect the experience of Adolph (1951) has been nply confirmed in our series, and there is good reason believe that it has been confirmed in man (S Kaplan d B A. Cookson, personal communications) The idence of ventricular fibrillation may confine the plication of deep hypothermia to a very limited age oup and mild hypothermia in combination with a chanical oxygenator (Melrose 1953) may become the hnique of choice in older children and in adults

Conclusions

From this investigation certain tentative conclusions ay be drawn for the use of hypothermia in surgery

(1) The particular method used to lower body tem rature is not of great importance but of the various ans available surface cooling is the simplest

(2) Until some method is found of preventing ven cular fibrillation the body temperature should not reduced below 26°C, and in all cases in which hypo rmia is used continuous electrocardiograms should displayed

(3) Hypothermia may offer an advance in surgery for erations requiring temporary occlusion of the great sels, but the increased irritability of the cardiac scle at temperatures of 25 C and below is the chief k of operations on the heart under these conditions

(4) The age of the animal is of particular importance the younger the animal the greater the margin of fety

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NECROTISING ENTERITIS FOLLOWING GASTRIC SURGERY

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During the last five years 10 cases of severe diarrhœa, associated with circulatory collapse occurring two or three days after operations on the stomach, have been observed in this hospital Of these 10 patients 5 have died, and in each case necropsy has shown necrosis of the mucosa of the small bowel. The clinical course of the 5 survivors was so similar that it seems reasonable to treat them as a homogeneous group and to assume that the pathology is the same.

Such a condition is not new, and 2 cases of Riedel's (1902) one following a high subtotal gastrectomy for carcinoma, and the other a Billroth I for benign stricture seem to be typical.

The subject has been reviewed by Penner and Bernheim (1939) and Penner and Druckerman (1948) who give an admirable historical survey Further cases following various operations are reported by Dixon and Weismann (1948) from the Mayo Clinic But we have been unable to trace any recent records in the English literature.

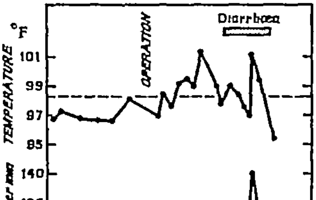


Fig 1—Chart of case 1 showing reactions to pulmonary atelectasis on second day and to necrotising enteritis on third day after operation

Case records

Case 1 —A Billroth I type of partial gastrectomy was performed on a fit man, aged 51 for a long-standing gastric ulcer No particular difficulties were encountered at the operation, and his immediate postoperative condition was satisfactory Next day, however, he had the signs of pulmonary collapse at the left base associated with a rising temperature, pulse rate, and respiration rate (fig 1) This responded to routine treatment, and on the morning of the third postoperative day his temperature had returned to normal and the signs in his chest cleared Gastric aspiration and the administration of rectal fluid were stopped By then, however, he was complaining of epigastric colic His abdomen was distended, but bowel sounds were present That evening his temperature, pulse rate, and respiration rate rose sharply, and he passed five very offensive loose motions Early next morning (fourth postoperative day) his condition was desperate he was cyanosed and dyspnœic, and his blood pressure was unrecordable He died at 11 P.M., eighty four hours after the operation, having had profuse diarrhœa during the day He was considered to be a case of bilateral pulmonary collapse, and his rate of decline was so rapid that no explanation of the abdominal symptoms was reached and no intravenous fluids were given

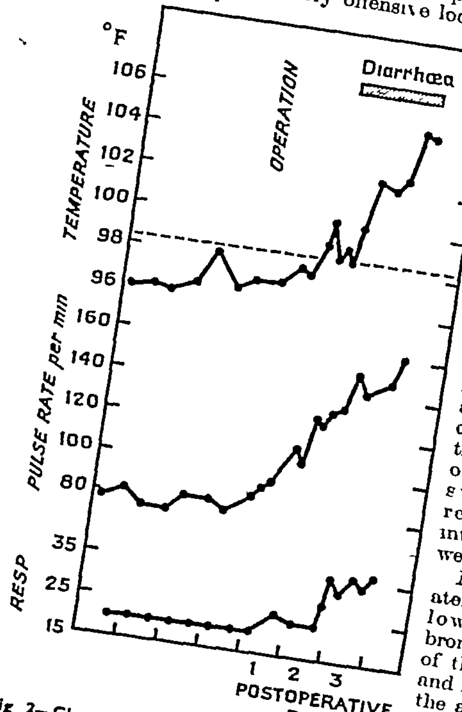


Fig 2—Chart of case 3 showing reactions on evening of first postoperative day to necrotising enteritis

Necropsy showed atelectasis of both lower lobes with bronchopneumonia of the right upper and lower lobes In the abdomen there was no peritonitis and the anastomosis was intact but in the upper half of the small intestine the mucous membrane had sloughed leaving only a few adherent white shreds

This may be regarded as a typical case of the condition under discussion The points to be noted are

A gastric operation is performed on a fit person and followed by an uneventful immediate postoperative course of about two days (though in case 1 it was complicated by a transient pulmonary collapse) On about the third day the patient complains of colicky epigastric pain, accompanied by abdominal distension, with normal bowel sounds He develops severe offensive diarrhœa, becomes dehydrated, and passes into circulatory failure, associated with fever, tachycardia and cyanosis In the absence of suitable treatment death is rapid Necropsy shows very little apart from the sloughing of the mucosa from various parts of the small intestine There is no peritonitis

The main points of the 9 other cases are as follows

Case 2—A partial gastrectomy was done in a patient, aged 38, who had unsuccessfully undergone vagotomy and gastro-enterostomy previously The operation was difficult and long, and the patient was shocked on returning to the ward but responded to blood transfusion His condition was satisfactory until the evening of the second day when he complained of colicky epig[illegible] pain His abdomen was distended, and bowel sounds were present He vomited once and developed offensive diarrhœa, which continued for twelve days, 50–100 oz. of fluid being passed a day Fluids, including plasma, were replaced intravenously throughout this time, and he made a good recovery and suffered no late ill effects, apart from homologous serum jaundice three months later

Case 3—Vagotomy and gastroenterostomy was performed on a fit man, aged 47, for duodenal ulcer, without difficulty His condition was satisfactory until the evening of the first day, when his temperature, pulse rate, and respiration rate rose (fig 2) Next morning he deve diarrhœa, and by the second evening his blood pressure dropped to 80/50 mm Hg An intravenous infusi saline was started but he remained in "circulatory colla and died within six hours, three and a half days operation

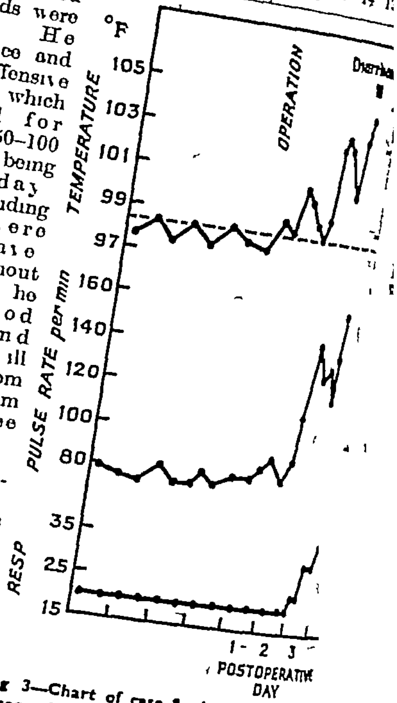


Fig 3—Chart of case 8 showing reaction second postoperative day to enteritis

Necropsy showed sloughing of the mucosa from the intestine from 30 cm below the anastomosis to 50 cm. the ileocæcal valve There were no other findings of no

Case 4—A fit man, aged 44, developed offensive dia with a rising pulse rate on the third day following a Bil type of partial gastrectomy for gastric ulcer, which pre no particular difficulties He was treated energetically intravenous fluids and made an uneventful recovery diarrhœa had ceased on the sixth postoperative day

Case 5—A Polya type of partial gastrectomy was perf with some difficulty on a fit man, aged 30, for duodenal His immediate postoperative course was uneventful, the evening of the third day he developed colicky ep pain with abdominal distension and a pulse rate of 1 temperature of 101°F Bowel sounds of normal quality present Next morning he developed profuse offensive rhœa and throughout the day he continued to be in circulatory collapse until the evening, when he died, 10 after operation 2 litres only of saline solution was intravenously during the last nine hours *Necropsy*

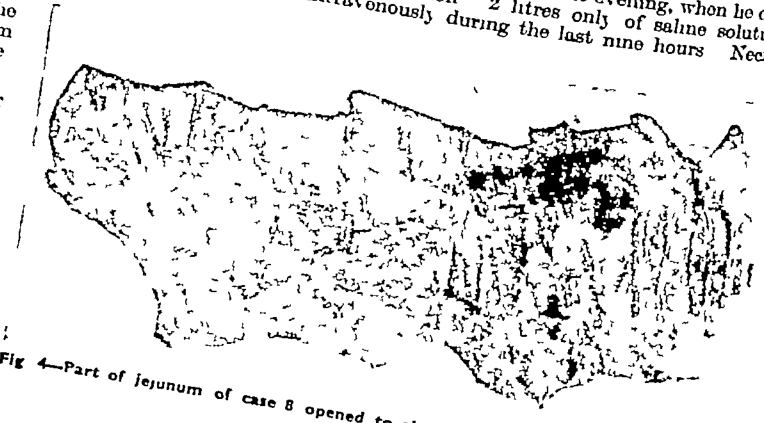


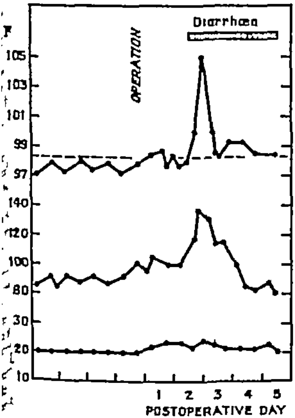
Fig 4—Part of jejunum of case 8 opened to show necrotic mucosa separating as a slough denuding the submucosa.

peritonitis and the suture lines were intact. The jejunum d ileum were distended with fluid The mucosa of the um was necrotic and had formed a tubular cast The ange in the mucosa of the jejunum was more patchy and ged strips of mucosa were loosely adherent to the bowel ll The colon was normal

Case 6 —A fit man aged 43 underwent an antecolic Polya pe of partial gastrectomy for chronic gastric ulcer His mediate condition was satisfactory but on the evening of third day he developed diarrhœa with a temperature of °F The diarrhœa continued five times daily for two days s fluid balance was maintained with intravenous saline ution and glucose He made an uneventful recovery

Case 7 —A Bilroth I type of partial gastrectomy was done an emphysematous but otherwise fit man, aged 65 for nign gastric ulcer On the evening of the first postoperative y he was distended and complained of epigastric colic On second day he was very ill and dehydrated his abdomen s distended but the bowel sounds were present and normal ur offensive fluid motions were passed Preliminary intra nous therapy was started, but was discontinued, after only 0 ml had been given owing to sacral œdema On the third y only 180 ml. of urine was passed in the twenty four hours, d the blood urea level was 173 mg per 100 ml (preoperative el 25 mg per 100 ml) On the fourth day the general dition improved after the administration of 4 litres of 3% line solution intravenously but next day auricular fibrillation developed and the patient died in a state of circulatory collapse on the evening of the sixth day

Necropsy showed that from a short distance below the duodenum the mucosa of the entire small bowel was congested and in places desquamated to form a cast There were also several discrete hæmorrhagic ulcers. These changes extended to the ileocæcal valve and increased in intensity distally The whole small intestine was distended with gas and large quantities rown fluid. The large bowel showed similar though much intense change. There were no other findings of note



5—Chart of case 9 showing reactions to crotising enteritis on second postoperative day d rapid improvement on rehydration on rning of third day

ase 8.—An anterior Polya type of partial gastrectomy done on a fit man aged 54 without incident. Apart from inent pulmonary atelectasis his condition was satisfactory il the evening of the second day when he complained of ere colicky epigastric pain associated with abdominal ension and active bowel sounds. His chart was typical 3). By next morning he was in severe circulatory collapse a diagnosis of internal hæmorrhage was made 2 pints h of dextran and blood were rapidly infused without evident efit. Only then did the passage of one offensive fluid motion l to a correct but belated diagnosis, and 4 litres of avenous glucose or of saline solution was administered. patient rallied for a little, but died eighty four hours after operation.

t *necropsy* the suture lines were healthy and there was no tonitis. The stomach, duodenum, and upper small bowel greatly distended with fluid From 1 in. below the stomosis and for the next 4 ft the jejunal mucosa was rotic and in most places separated as a yellow opaque gh (fig 4) In places this was adherent but the greater part lay free as a bolus in the lumen some 8 ft from the anastomosis The denuded surface was red raw and granular The large intestine contained at least 2 litres of watery brown fluid There were no other changes of note

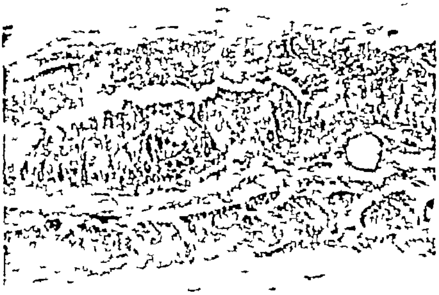


Fig 6—Section of small bowel showing necrosis of superficial glands of mucosa, with separation starting and survival of some glands in deeper parts. (Hæmatoxylin and eosin. × 33.)

Case 9 —A palliative partial gastrectomy for carcinoma of the stomach was performed without difficulty on a woman aged 53 Her condition was satisfactory until the afternoon of the second day when she developed colicky abdominal pain with sweating and very profuse offensive diarrhœa, passing 5 litres in two hours. She quickly passed into circulatory collapse and her temperature chart is shown in fig 5 Her diarrhœa continued to be very profuse Necrotising enteritis was diagnosed and intravenous glucose and saline solution were given as quickly as possible 10 litres was given in three hours and after this her condition rapidly improved and her temperature dropped dramatically A total of 16¹/₂ litres of saline solution and 2 pints of blood were administered in twenty four hours The diarrhœa decreased for eight days, and hydration was maintained by intravenous fluids The patient made an uneventful recovery and showed no late effects of the small bowel lesion

Case 10 —A rather wasted man aged 61 underwent operation for what was clinically thought to be a carcinoma of the stomach but proved to be a benign gastric ulcer A Polya type of partial gastrectomy was done without difficulty His condition caused no anxiety until the third day when he

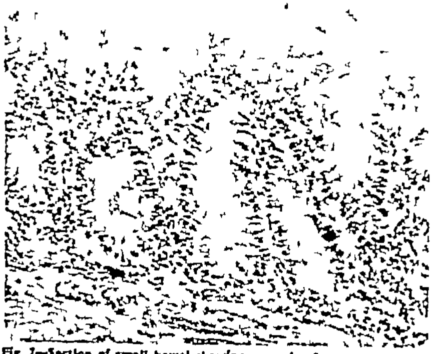


Fig 7—Section of small bowel showing necrosis of mucosa but little change in submucosa. (Hæmatoxylin and eosin. × 112.)

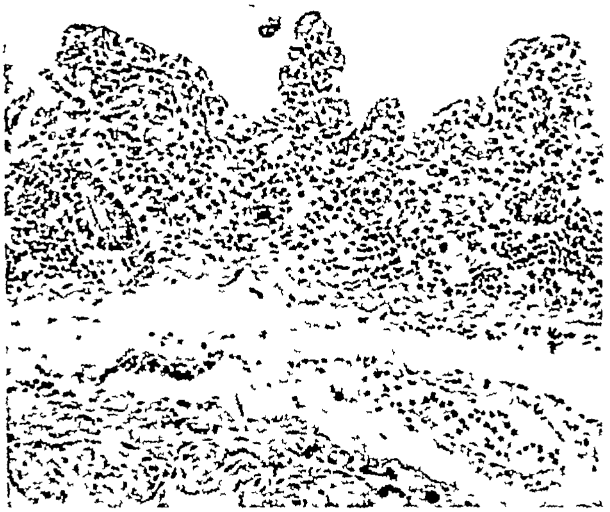


Fig 8—Section of small bowel showing necrosis of superficial layers of mucosa, with survival of isolated glands (Hæmatoxylin and eosin × 112.)

developed epigastric colic and a distended abdomen with active bowel sounds He also passed five offensive loose stools $2^1/_2$ litres of saline solution and 1 pint of plasma were given during the next twenty four hours This proved inadequate, and by the afternoon of the fifth day the patient was cold, cyanosed, and in circulatory collapse 4 litres of intravenous saline solution was then given in five hours, and his condition rapidly improved A further $5^1/_2$ litres of saline solution and glucose was run in during the next twenty four hours. He made an uneventful recovery, the diarrhœa finally settling on the ninth day

Discussion

The clinical picture of a patient who, on the second or third day after a gastric operation, develops colicky epigastric pain, abdominal distension with active bowel sounds, and raised temperature, pulse-rate, and respiration rate, and proceeds to profuse offensive diarrhœa and severe vascular collapse is unmistakable when presented in a series like this In many ways the condition is analogous to cholera and requires similar restorative therapy Some of these cases have been mistaken for pulmonary atelectasis, leak at the anastomosis, paralytic ileus, or internal hæmorrhage If, however, the condition is recognised and adequate fluid is promptly replaced intravenously, the patient immediately improves This may involve the rapid infusion of very large quantities of fluid In the last 3 cases intravenous aureomycin has also been given, for reasons discussed below, but this is of doubtful value In patients who recover, the diarrhœa stops after about a week, and in none of the surviving patients had there been any late complications In 2 of them the small bowel pattern shown by barium was normal before discharge from hospital

PATHOLOGY

The pathology of the fatal cases is equally consistent In all 5 of them the necropsy findings, apart from the lesions in the small intestine, were insignificant There was no peritonitis, and the anastomoses appeared healthy The external appearance of the small bowel was unremarkable, and there was no obvious enlargement of the mesenteric glands In every case, however, when the small bowel was opened, it was found that the mucosa had sloughed to form a membrane, which had either completely separated and passed down the gut or was still partly attached to the remaining bowel wall This necrosis is often patchy and more severe in some s than in others (fig 6) It had usually started some distal to the anastomosis, and the extent of the bowel affected varied, but in no case did the necrosis encroach on the anastomosis

Sections from the wall of the bowel in the diseased portions show that the necrosis is limited to the mucosa and that the submucosa is relatively normal (fig 7 Further, although the superficial layers of the mucosa glands have died, there are numerous little patches of surviving basal cells (fig 8) In other words, the condition is analogous to partial thickness skin loss and is equally recoverable

Cellular infiltration is remarkably slight and consists largely of cells of the histiocyte and lymphocyte series, polymorphs being scarce The appearance of the submucous and muscular layers is normal (fig 9)

In 8 cases either the stools in vivo or the small-bowel content post mortem were examined bacteriologically In 2 (cases 4 and 10) no pathogens were found in the stool The small-bowel contents were cultured post mortem in cases 1, 5, and 7, and grew *Bacterium mucosum capsulatum* and enterococci, hæmolytic streptococci, and proteus respectively *Staphylococcus aureus* was found in the small-bowel contents in cases 3 and 8, and in the stools of case 9 Cases 8 and 9 occurred within a week of each other but with different surgeons and in different wards The organisms from these 2 cases were typed and found to be 52A and 6/47 respectively Stools were obtained from 14 patients in the same ward as case and cultured on a salt containing medium In 6 *Staph aureus* was grown and typed, yielding three of 52A, two of 76/77, and one of 6/47 Stools from ward-mates of case 9 yielded two positive cultures of staphylococci but unfortunately were not typed

The stomach and small bowel and nose of case 9 were swabbed at the time of operation None of these swabs yielded *Staph aureus*, though her stools yielded staphylococcus during the acute episode. There was no organism common to all the cases, and staphylococci of the same phage type were not uncommon in unaffected patients

It seems likely, from the very heterogeneous collection of organisms obtained, that they are in fact incidental

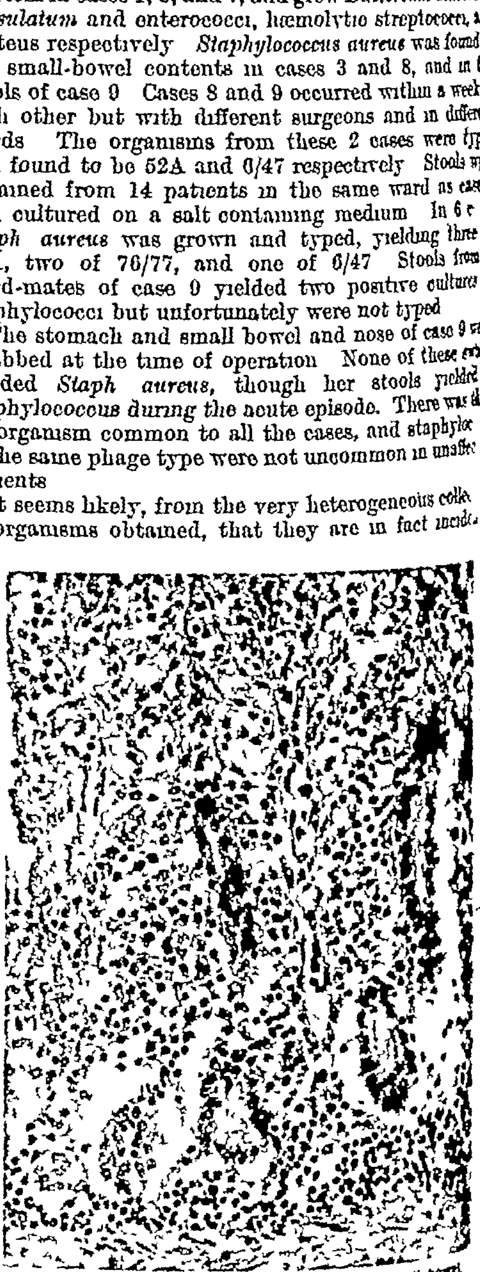


Fig 9—Section of deeper portion of submucosa of small bowel showing predominance of round cells and absence of pol (Hæmatoxylin and eosin × 230)

ANALYSIS OF CASES

Sex	Age (yr)	Disease	Preoperative drugs	Operation	Postoperative drugs	Day of onset of symptoms	Culture of stools	Result
M	51	Gastric ulcer	Sulphamerazine	Billroth I	Sulphamerazine	3rd	*Bact. mucosum capsulatum* and enterococci	Died
M	38	Gastric retention following vagotomy and gastro-enterostomy for duodenal ulcer	Sulphamerazine	Polya type	Nil	2nd	Not cultured	Survived
M	47	Duodenal ulcer	Sulphamerazine	Vagotomy and gastro-enterostomy	Penicillin	2nd	*Staph. aureus*	Died
M	44	Gastric ulcer	Nil	Billroth I	Penicillin	3rd	Not cultured	Survived
M	30	Duodenal ulcer	Nil	Polya type	Nil	4th	Hæmolytic streptococci	Died
M	43	Gastric ulcer	Nil	Polya type	Nil	3rd	Not cultured	Survived
M	65	Gastric ulcer	Sulphamerazine Penicillin	Billroth I type	Penicillin	2nd	Proteus	Died
M	54	Gastric ulcer	Nil	Polya type	Streptomycin	3rd	*Staph. aureus*	Died
F	53	Carcinoma of stomach	Nil	Polya type	Streptomycin Penicillin	2nd	*Staph. aureus*	Survived
M	61	Gastric ulcer	Nil	Polya type	Nil	3rd	*Staph. aureus*	Survived

d not an ætiological factor in the enteritis, a supposition pported by the histological picture which is not that an acute infection. Nevertheless antibiotics should bably be given if only to protect the denuded bowel ing

TREATMENT

ince the primary pathological lesion is a surface truction of the mucosa of the small bowel followed a massive exudation and loss of fluid into the lumen essential disturbance in these patients is dehydration e total fluid loss may of course be very much greater n that suggested by the volume of vomit or fluid ols since the distended bowels may contain several es. Indeed case 8 was severely shocked from dehydra n for eight hours *before passing a fluid motion*

he emergency treatment is to replace intravenously lost water as rapidly as possible, along with sufficient s or glucose to render it isotonic The fluid volume uired may be very large, and the sign that sufficient eing given is the clinical improvement in the patient. blood pressure rises his temperature and pulse rate and he becomes more coöperative and less cyanosed ce the infusion may be running at the rate of up to tres an hour it is easy to overload with sodium A table plan is 1 litre of physiological saline solution to itres of 5% dextrose until rehydration has been ered. After this, hæmatocrit readings and estimations erum-electrolytes (sodium chloride, and potassium) show what extra ions, if any should be given to ect the balance There is also loss of protein which be corrected by transfusions of blood or plasma, and s probably wise to incorporate at least 2 pints of um in the initial phase provided this does not rfere with the rapidity of infusion

nce a balance has been achieved the emergency has sed, and fluid requirements can then be estimated in normal way

RELATED CONDITIONS

enner and Bernheim (1939) and Penner and Drucker a (1948) describe a condition which appears to be y similar to the one described here and follows various rations and is also found in medical cases—i.e., petic coma In particular they record 2 cases following trectomy which are readily comparable to the present es. In both of them the blood pressure fell considerably ing the operation (to 48/30 mm Hg and 80/50 mm and they regard this as an ætiological factor They believe that the mechanism is a compensatory spasm in the vessels of the submucosa giving rise to multiple focal areas of necrosis. They describe patches of local œdema in the submucosa with dilated capillaries, progressing to extravasation, and necrosis of the overlying tissue. In our series significant falls in blood pressure did not occur during operation, except in cases 2 and 5 Also in our histological material the changes in the submucosa consist only in dilatation of the capillaries and these appear to be secondary to the other changes rather than primary

Dixon and Weismann (1948) described 23 cases, in 15 of which, however, the picture is confused by the presence of peritonitis In the remainder an analogous condition seems to have followed colonic surgery The intestinal lesions tended to be more widespread often involving the œsophagus and colon, and the onset of the complication was rather later We have been unable to trace any similar cases at this hospital. Many of Penner's cases seem to belong to this group also

Another condition which clinically resembles the present cases is the epidemic necrotising enteritis which occurred in the summer months in North west Germany after the war (Fick and Wolken 1949)

> Severe cramping epigastric pain comes on suddenly in a previously fit person, and is associated with profound circulatory collapse. The patient may die in twenty four hours; if he survives longer he will have profuse bloody diarrhœa
>
> The necropsy findings in the small intestine differ considerably from those of our cases, for the jejunum is turgid and sausage-shaped with a bright-red serosa. The swelling is due to gross œdema, which also reduces the lumen.
>
> The mucosa forms similar sloughs and histologically seems to be analogous. In these cases the necrosis goes deeper and may lead to perforation with peritonitis. Recovery is complicated by stenosis.

Two similar cases have been described in England (Greville Young 1949 Calnan 1950) Suggested ætiological factors are (1) malnutrition, which is not applicable to our cases with the possible exception of cases 9 and 10 and (2) acute infection due to *Clostridium welchii* type F (Zeissler and Rassfeld Sternberg 1949) No investigation on these lines was made in our cases.

ÆTIOLOGY

The ætiology of the present series of cases is obscure. Most of the patients were fit and well nourished before operation. Apart from 2 cases there were no operative difficulties and no gross fall in blood pressure The conditions for which operation was performed were various (see table) Some of the patients had sulphonamides and antibiotics preoperatively, but most did not Some of them had antibiotics postoperatively and some did not The patients were operated on by eight different surgeons using different techniques The sparing of the gastric mucosa and that of the jejunum or duodenum adjacent to the stoma is constant and seems to exclude operative trauma as a starting point for the necrotising process At least 1 operation was done without clamps All types of suture materials were used The patients were nursed in different wards, and the operations were done in different theatres The bacteria flourishing in the small bowel were of different types, but the clinical picture and necropsy findings remain extremely constant

Although the ætiology is unknown, the clinical picture is sufficiently characteristic to provide the diagnosis and to indicate treatment which, if adequate and prompt, will ensure a happy outcome in a desperate condition

Summary

Ten cases are described in which a characteristic syndrome developed after gastric surgery

Five of the patients died, and necropsy showed that, in all of them, the small intestinal mucosa had sloughed over a considerable area

The diagnosis, treatment, and ætiology are briefly considered

Our thanks are due to those members of the staff of St Thomas's Hospital who have given permission for us to include some of their cases

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GROWTH OF CLOSTRIDIUM WELCHII IN THE STOMACH AFTER PARTIAL GASTRECTOMY

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During the first week after the operation of partial gastrectomy, often between the third and fourth days, a few patients develop diarrhœa which is usually mild and ceases within twenty-four hours, but is occasionally more severe In attempts to discover a bacteriological cause for the diarrhœa, the fæces of such cases were repeatedly examined in this laboratory without disclosing the presence of specific intestinal pathogens During the past few months examination of the stools and paired sera of 5 cases of diarrhœa after gastrectomy failed to reveal any evidence that the diarrhœa might be due to serological types of *Escherichia coli* associated tro-enteritis

Recently, we were impressed by the similarity of the clinical symptoms of post gastrectomy diarrhœa and of the gastro enteritis caused by food poisoning with heat-resistant *Clostridium welchii*, type A (Hobbs et al 1953, Oakley and Warrack 1953) We did not find heat-resistant *Cl welchii* in the fæces of patients after partial gastrectomy, whether they had diarrhœa or not, but we found numerous *Cl welchii* during the first week after partial gastrectomy in the stomach contents of 11 of 15 patients examined Moreover, in 8 of the 15 patients filtrates of the stomach contents contained detectable amounts of the α toxin of *Cl welchii* Such an observation does not appear to have been made before, so we think it worth recording a brief account of our findings at this stage

Material and Methods

Patients

All 15 patients were in the wards of the Western Infirmary of Glasgow under the charge of Prof C F W Illingworth Through his coöperation and the ready assistance of his medical and nursing staff specimens of stomach contents were collected and sent at once to the laboratory for examination Of the 15 patients 12 had partial gastrectomy, with retrocolic anastomosis of the stomach remnant to the jejunum, for gastric or duodenal ulcer, 2 had the same operation for the same cause but with antecolic anastomosis, and 1 had a total gastrectomy with retrocolic anastomosis for carcinoma of the stomach Only 1 of the 15 patients suffered from postoperative diarrhœa, the patient affected having four loose motions on the third day and three on the fourth day after operation None of the others showed any unexpected signs or symptoms during convalescence and all recovered from the operation After operation a Ryle's tube was left in the stomach which was aspirated by continuous suction for twenty-four hours, during which period only water was taken by mouth During the next twenty four hours diluted boiled milk was given by mouth, thereafter undiluted boiled milk was given

Specimens from Stomach

Specimens from the stomach were aspirated by a syringe attached to the proximal end of a Ryle's tube. 5–20 ml of fluid mixed with mucus was generally obtained, but 7 specimens from 6 patients could be withdrawn only after 5–10 ml. of saline had first been injected into the stomach through the tube In all, 28 specimens were collected from the 15 patients between the first and fourth days after the operation of partial gastrectomy

Films and Cultures

The specimens of stomach contents were centrifuged and films of the deposits were examined by Gram's method, a few were also examined by the eosin method for the demonstration of capsules One loopful of each deposit was spread on each of two blood-agar plates which were incubated at 37°C, one aerobically and the other anaerobically in a McIntosh and Fildes jar One drop (cases 1–6) or several drops (cases 7–15) were also inoculated into a tube of Robertson's meat broth, which was put in the incubator under ordinary atmospheric conditions

Determination of pH

The pH of each sample of stomach contents was determined by indicator papers checked at frequent intervals with a glass electrode and a Doran pH meter

Examination of Filtrates for Welchii Toxin

The supernatant fluid of the centrifuged stomach content was passed through a Seitz sterilising or clarifying (F C B) disc and examined for welchii α toxin by the lecitho vitellin (L V) and the hæmolytic tests, the methods followed being those described for culture filtrates by Oakley and Warrack (1953) f the fluid was more acid than pH 6·5 a few drops of N NaOH were added to bring the reaction between pH 6·5 l 8·0. If the fluid was hypotonic as roughly tested by ding a loopful on a slide with a loopful of red-cell suspension, Cl was added to make it isotonic. 1 ml. of filtrate of the mach content was then put into each of 4 tubes. Of se tubes 1 and 3 received also 0·5 ml. of saline and tubes 2 l 4 received 0·5 ml. of *welchii* α antitoxin diluted to contain units per ml. To each of the 4 tubes 0·5 ml. of borate fer saline with calcium chloride and peptone was added contents were mixed and the tubes were left on the bench 30 minutes. The composition of the borate buffer saline in 1 litre of distilled water) was: borax 3·55, boric acid 5, sodium chloride 0·2, calcium chloride 0·5, and peptone 0. The pH was 8·0–8·4. Tubes 1 and 2 then received ml. of L.V. suspension; tubes 3 and 4 received 0·5 ml. washed sheep red cells suspended (6% suspension) borate buffer saline. The tubes were then incubated in a ter bath at 37°C for one hour and read after standing over ht on the bench at room temperature. The filtrate was orded as containing *welchii* α toxin if tube 1 showed opacity tube 3 showed hæmolysis or if hæmolysis and opacity re both observed. Tubes 2 and 4, the control tubes taining antitoxin, showed neither opacity (tube 2) nor molysis (tube 4).

Culture filtrates of *Cl. welchii* isolated from the mach contents were titrated for *welchii* α toxin by molytic and L.V. tests by the methods described by kley and Warrack (1941).

titoxin in Patients' Sera

Paired sera were taken from 13 patients, the first ecimen on the day before operation and the second between the seventh and tenth day after operation. After being heated at 56°C for 30 minutes they were examined for *welchii* α antitoxin by the methods described by Oakley and Warrack (1941).

BLE I—EXAMINATION FOR *Cl. welchii* AND ITS α TOXIN N THE STOMACH CONTENTS AFTER PARTIAL GASTRECTOMY

Day after gastrectomy	pH of stomach contents	Examination of stomach contents				
		For *Cl. welchii*			For *welchii* α toxin	
		In films	On blood-agar	In meat broth†	Lecitho-vitellin test	Hæmolytic test
1	6·7	+	+	−	−	
2	7·0	+		−		−
3	3·5	+	−	−	−	−
1	1·0	+	−	−	−	−
4	3·1	−	−	−		+
1	3·5	−	+	−	+	+
3		−	+			
[illegible]	−	+	−		−	+
1	4·0	−	−	−		+
3	5·0	++	−	+	−	−
1	3·5	+	−		−	−
2	5·0	+	−	−	−	−
1		+	−			
[illegible]	3·1	+	−		−	−
1	6·4	−	+	+	+	+
1	6·7	+		+	−	+
2	7·3	−	−		−	−
3	1·0	++	+		−	−
1	6·5	−	+		−	−
4	5·0	++	+		−	−
[illegible]	8·4	−	−	+	−	−
2	6·7	−	−	−		−
3	5·0	+	+	+	−	−
1	3·1		−	+	−	
1	7·0	−	−	−	+	Unsuitable‡
1	3·5	+	−		−	
	6·6	+	−	+	−	+
4	6·7	++	−	+	−	+

cimen diluted in saline solution.

cases 1–6 the meat broth was inoculated with 1 drop of material. In cases 7–15 several drops were used.

ecimen contained lysed blood and so was unsuitable for hæmolytic test.

o observation.

TABLE II—TOXIN PRODUCTION IN BROTH SUBCULTURES OF SIX STRAINS OF *Cl. welchii* ISOLATED FROM STOMACH CONTENTS AFTER PARTIAL GASTRECTOMY

Strain no.	Minimum opacifying dose of filtrate in L.V. test (ml.)	Minimum hæmolytic dose of filtrate (ml.)	α-antitoxin equivalent of filtrate by hæmolysin titration (units per ml.)
40	0·05	0·01	0·2
43	0·25	0·25	0·01
46	0·25	0·01	0·03
50	> 10	1·5	0·002
54	0·25	0·05	0·05
58	0·25	0·05	0·03

Results

The results of our examinations, which could not be correlated with any particular clinical symptoms, signs, or events, are summarised in table I.

Presence of Cl. welchii

Direct films of the centrifuged deposits of the stomach contents of 12 of the 15 patients and 17 of the 28 specimens contained many gram-positive rods which sometimes appeared singly but more often in clumps and short chains. Many of the forms were relatively short and stout, about 3–4 × 1 µ. Their appearance suggested a diagnosis of *Cl. welchii*, a possibility which was strengthened when the first specimens were examined and found to have capsules surrounding the bacilli. Cultures on the positive anaerobic blood-agar plates yielded typical *Cl. welchii* colonies surrounded by zones of clearing. The identity of the organisms was confirmed by their production of *welchii* α toxin in broth subcultures. So far the organisms have not been examined for production of other *welchii* toxins or for the heat-resistance *of their spores in cultures. Heat-resistant Cl. welchii* were not found in the fæces of a few cases examined for this point.

Demonstration of Cl. welchii *α Toxin in the Stomach Contents*

When films and cultures revealed the presence of *Cl. welchii* in the stomach contents, the question arose whether the organism was merely a transient or whether it must be regarded as colonising the stomach remnant. In considering this point it was obviously of interest to discover if toxin was produced, and our findings show that it was. The stomach contents of case 4, that of the only patient who suffered from postoperative diarrhœa, did not yield demonstrably more toxin than the stomach contents of the others who had no diarrhœa.

Table I shows that the L.V. test was positive in only 3 of the 10 specimens in which toxin was demonstrated. The first specimen from case 14 contained lysed blood and so could not be used for a hæmolytic test; it gave a positive L.V. reaction. 2 positive filtrates were diluted and examined by the hæmolytic test to find how much toxin they contained. Evidently the amount was only about 1 minimum hæmolytic dose per ml., because even when diluted only 1 in 2 these filtrates yielded a negative result. Not enough filtrate was available from other positive specimens to titrate them in this way. The 2 specimens which gave a positive L.V. test and could be examined by the hæmolytic test were positive by that method also. The low ratio of positive L.V. tests to positive hæmolysin tests is probably explained by the small amounts of toxin present, for on titrating filtrates of subcultures of six of the isolated strains we found that the hæmolytic test as carried out

with borate buffer saline containing added calcium
chloride and peptone was a more sensitive indicator
than the L V test The details of toxin production by
these six strains (table II) show that the strains were not
ery active producers of α toxin The amounts pro-
uced may be compared to those found by Evans (1945)
r two strains from the human intestine—namely,
e α antitoxin equivalent of 0 05 and 0 03 unit per ml
obbs et al reported that their food poisoning strains
of Cl welchii, type A, produced only small amounts of
toxin in culture—never more than the equivalent of
one α-unit per ml and usually far less

Antitoxin in Patients' Sera

As already described, the sera of 13 patients were examined for *welchii* α antitoxin before and from seven to ten days after operation Titration was done by the hæmolytic method and the results were negative in that none of the sera showed as much as 0 002 unit per ml, the smallest amount measured by our tests Through the kindness of Dr C G Paine, Jessop Hospital for Women, Sheffield, we also examined serum taken from a woman eleven days after the onset of a severe post-partum infection with *Cl welchii* This serum contained only 0 005 unit of *welchii* α antitoxin per ml In the light of this low value after a severe infection the negative results in our patients are not surprising, particularly in view of the small amounts of toxin which we found in filtrates of their stomach contents

Discussion

The starting point of the present investigation was our inability to identify a bacterial cause for the diarrhœa, usually mild and transient, which sometimes complicates convalescence during the first week after partial gastrectomy Our results now show that this operation influences events within the human alimentary tract in such a way that *Cl welchii*, a normal inhabitant, may grow and produce detectable amounts of α toxin within the remnant In food-poisoning due to
the type normally found i
observations and references
establish that the symptom
type and duration to those
develop diarrhœa after gastre
significance of our observations it test the clinical
worth giving a dose of *Cl welchii* antitoxin to patients who would probably be about to undergo the operation of gastrectomy Analysis of the postoperative records of a series of cases given antitoxin compared with those of comparable cases not given antitoxin, together with the results of bacteriological examination, would probably show whether the growth and toxin production by *Cl welchii* after gastrectomy have any clinical significance or none Admittedly we found only small amounts of toxin in the stomach remnant, of the order of one hæmolytic dose per millilitre, and toxin was detected in only 8 of the 15 patients examined, but two points may be noted in this connection The first is that 7 of the 28 specimens examined were diluted with saline solution to withdraw them and that only 1 of these was found to contain toxin Since dilution of known positive specimens even to only 1 in 2 was enough to give a negative hæmolytic test, the dilution may be regarded as weighting events against our finding toxin in these specimens Moreover, the single positive among the diluted specimens was detected only when we used a Seitz clarifying (F C B) instead of a sterilizing (S B) disc, which we had previously employed Later, on passing through a Seitz S B disc 7–9 ml volumes of diluted toxin containing 20 or 100 minimum hæmolytic doses (M H D) per ml, we found that less than 1 M H D per ml appeared in the filtrate Even with an original concentration of 1000 M H D of toxin per ml the
so filtrate contained only 40 M H D per ml Use of

the F C B disc reduced the concentration from 20 to
M H D per ml, filtration through a 'Gradocol' membra
of 0 9 μ average pore diameter left the concentr
of toxin unchanged The second point is t
number of organisms and amount of toxin a
likely to be much greater in the ileum th
the stomach In sheep this concentration bo
organisms and of toxin in the ileum has been obs
both in natural and in experimental infections o
intestinal tract with *Cl welchii* type D (Bennetts
Bullen 1952, Bullen et al 1953) It is also of inte
that Bullen et al noted a violent though trans
of diarrhœa in one of eight experimentally infected
in which the concentration of *welchii* ε toxin i
ileum reached a level of 2000 mouse M L D per g
pared with values of 800 or fewer mouse M.L.D
in the other seven sheep If organisms and toxi
likewise concentrated in the human ileum this
explain why we found no greater amount of tox
stomach of our patient (case 4) who suffered
diarrhœa than in the others who did no

It is worth noting that enterotoxæmi
is caused by the ε toxin of *Cl welchi*
easily reproduced experimentally Suc
have been attributed to administration
with belladonna and opium to paralyse
ment (Bennetts 1932) and of milk to fa
the organism (Roberts 1938, Harshfield
After partial gastrectomy intestinal
temporarily reduced and the patients are
diet It may be that these circumstan
together in our cases to favour the growt
production by *Cl welchii* which we observed

In the past, a great deal of attention was
possibility that toxin production by *Cl we*
human intestine migh
see, for
athological sig
26–27), Davids
nberg (1929),
Bower et al
944) also show
agonal invasion found post mortem
estinal organisms, probably *Cl welchii* of the blood by

Much of the earlier work suffered from
difficulties of demonstrating and measuring *welchii*
and its antitoxin and of legitimate doubts about
interpretation of some at least of the results—diff
and doubts now able to be resolved by the
of the hæmolytic and lecitho vitellin
seems to us that our evidence makes a case
the position again

Summary

In 12 of 15 patients examined during the fir
the operation of partial gastrectomy numerous
welchii were found in films and cultures from t
contents In 8 of the 15 patients small
welchii α toxin were also demonstrated in
specimens

It would probably be worth investigatin
influences favour the development of *Cl welch*
gastrectomy and whether there is any clinical sig
in growth and toxin production by the
the circumstances described

The use of the hæmolytic and lecitho-vitellin
of titrating *welchii* α toxin and antitoxin could
many of the difficulties of technique and doubts
interpretation associated with earlier work which
to establish the rôle of *Cl welchii* as a human
pathogen

We are grateful to Prof C F W Illingworth for dr
our attention to this problem, to Professor Illin
medical and nursing staff for their trouble in collecting
mens for us, particularly to Mr J K Watt whose

the work was of great value, especially at its beginning Miss Mollie Barr Mr H. Proom and Prof. C. L. Oakley gifts of standard materials and for helpful information methods; to Dr Joan Taylor for examining strains of coli; and to the Medical Research Council and the nkin Fund for grants towards the expenses of the estigation.

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CHÆMIC NECROSIS OF THE STOMACH

FOLLOWING SUBTOTAL GASTRECTOMY

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F the many possible complications of subtotal gas tomy one is so rarely described that few surgeons sider it in planning their operation This complication schæmic necrosis due to over enthusiastic devascular ion of the proximal part of the stomach Careful ch has revealed no reported instance of this com ation during the past twenty years The following rt of a fatal case is a reminder that the blood supply he stomach cannot be interfered with so lightly as ent teaching might lead one to expect.

Case record

he patient was a man, aged 40 who had had intermittent epsia of characteristic ulcer type since 1945 Gastric r had been demonstrated radiographically in 1946 and ad had two periods of thorough inpatient medical treat t in other hospitals Each period of treatment had ight about remission followed after a few months by rrence of symptoms. Severe symptoms began again at nd of 1952; these did not respond to treatment at home he was admitted to Queen Mary s Hospital, Roehampton, Feb 18 1953

he patient was well built and healthy looking, with signs ild chronic bronchitis He was having severe almost inuous epigastric pain radiating through to the back. was sleeping poorly on account of the pain, which was not ved by taking either food or alkali The upper abdomen tender and muscular rigidity was quite distinct After a days on a régime of sedatives and two hourly milk feeds, pain was less severe; X ray examination now showed a deep ulcer high up on the posterior wall of the stomach. ther medical treatment including later an intragastric produced only very incomplete relief of his pain and rgical treatment was decided on.

operative biochemical examinations showed normal es for blood urea, chlorides, and protein and a red d-cell count of 3 000 000 cells per c.mm. with hæmoglobin The anæmia was corrected by transfusion of three s of stored whole blood and protein hydrolysates were both by mouth and parenterally during the days before ation.

eration was done on March 25 under nitrous-oxide/ opropane anæsthesia, supplemented with pethidine and *d* tubocurarine chloride The abdomen was opened through a left paramedian incision, and a large penetrating ulcer of the posterior wall of the stomach was immediately palpated; this formed a hard indurated mass of tissue infiltrating into the lesser omentum almost up to the level of the cardia. Glands in the lesser omentum were soft and fleshy and the lesion was judged to be benign and resectable The duodenum was healthy This was divided but not closed, and the ulcer was dissected off the pancreas with the diathermy knife, leaving a good deal of the ulcer base in situ. The left gastric artery was divided near its origin from the cœliac axis. The whole of the lesser curvature was necessarily removed for the ulcer was close to the œsophago-gastric junction and the greater curvature was very extensively mobilised to allow the gastrectomy to be completed by a Billroth I type of gastro-duodenal anastomosis. A tube drain was placed in the region of the ulcer bed on the pancreas, and brought out through a stab wound in the left flank. The operation was difficult but not unduly so and the patient left the operating theatre in excellent condition

Postoperative Course.—The patient s condition was good until 8 A.M next morning when he complained of severe abdominal pain and rapidly developed the appearance of extreme shock There was no vomiting The abdomen was rigid but not distended. The cause appeared to be either partial dehiscence of the suture line—for which no adequate reason could be adduced—or acute pancreatitis due to damage to the pancreas during removal of the ulcer The patient s condition improved considerably in the next few hours, and his pain diminished so it was decided to treat him conservatively until the diagnosis became clearer

On the second day after operation he was much improved; his pulse rate was still 110–120 per minute but he had little pain and did not seem to be greatly distressed Aspiration through a Ryle s tube yielded only a few drachms of slightly bloodstained fluid

On the third day there was some clear fluid discharge from the drainage tube the abdomen was much softer, but the pulse rate was still 110–120 per min Urinary output and fluid balance (by intravenous infusion of blood saline glucose and protein hydrolysate) were satisfactorily maintained

On the fifth day the discharge from the drainage tube became bile-stained and more copious the pulse-rate had fallen to 100 per min. and the patient s general condition was greatly improved. It was now fairly clear that some dehiscence of the anastomosis must have taken place; but as signs of general peritonitis were absent, and the patient s condition seemed to be improving no immediate surgical treatment was thought to be necessary

On the eighth day there was copious bile-stained discharge from the wound the pulse rate remained about 100 per min., and the patient s general condition was well maintained, though intravenous fluids were still necessary to achieve fluid balance and adequate caloric intake In order to elucidate the question of leakage from the anastomosis, a little dilute barium suspension was given by mouth and radiographs were taken with a bedside portable machine The barium appeared almost immediately in the discharge from the wound and the films showed a diffuse spread of the suspension in the left upper quadrant It was presumed from this that complete dehiscence of the anastomosis must have taken place and a further operation seemed inevitable However within a few minutes of taking the barium the patient suddenly collapsed again, with severe pain and profound shock and operation was obviously out of the question. After administration of morphine and blood transfusion he quite rapidly improved

Next morning—the ninth day after operation—he had apparently recovered completely from the attack The abdomen was soft and the pulse-rate only 96 per min., and he was quite free from pain the discharge from the wound was now very free and still contained traces of barium The sudden temporary collapse was attributed to the irritant effect of the barium suspension on the inflamed peritoneum

At a *second operation* on the evening of the ninth day the left paramedian incision was re-opened. The small bowel was not distended there were numerous plastic adhesions; a localised intraperitoneal abscess containing an ounce or two of pus was present Careful examination of the operation area showed that the duodenum right up to the suture line the stomach was normal and the suture line itself the œsophagus also appeared normal The wh stomach remnant was grey and avascular, and had the consistency of wet blotting paper There was a small perforation on the lesser curvature, and a much larger one on the greater curvature The latter perforation may have been made, or at least enlarged, by the manipulations necessary to inspect the stomach, for the gentlest handling of the stomach produced further tears in its wall No bleeding occurred from these tears Obviously the whole of the remaining stomach wall was necrotic, and any reparative surgery, at least at this stage, was out of the question An enterostomy was established in the first jejunal loop, and a further drainage tube inserted

Postoperative Course —The next day the patient appeared surprisingly well, the pulse rate was 120 per min, he was comfortable, and had passed some urine On the following morning—thirty six hours after the second operation and eleven days after the first—he collapsed, and he died in a few hours Necropsy confirmed the findings at the second operation, the duodenum and the œsophagus were healthy, but the whole of the stomach remnant was completely necrotic

Discussion

All current surgical textbooks describe in detail the blood supply of the stomach, and emphasise the richness of its anastomotic network All of them leave the impression that the arteries supplying the stomach may be divided just as far as is necessary to allow free mobilisation and adequate resection

Somervell (1946), describing his operation of "physiological gastrectomy," advised the division of "five out of six of the small arteries on the greater curvature and as many vessels as possible on the lesser curvature," but did not discuss what might happen if devascularisation were more complete Pannett (1938) advised the surgeon to divide the vessels "until he deems a sufficient length has been denuded, while Finsterer (1939) said that the stomach should be divided a hand's breadth to the left of its midpart, without specifying how far the vessels need be cleared Visick (1948), describing his "*measured radical gastrectomy,*" *stated that all but one* of the vasa brevia, and in certain cases all the vasa brevia, are to be divided, and he specified that "the line of section is made so as to leave a small *devascularised* remnant"

None of these workers suggest that there may be any danger in carrying the division of the vessels too high up the greater curvature The modern trend in gastrectomy has been towards higher and higher resections, and towards the removal of very high ulcers which might more safely be treated by resection below the ulcer (Wells 1933) Thus Hinton and Localio (1950), describing the technique of an operation for very high lesser curve ulcer involving the construction of a tube of greater curvature for anastomosis to the duodenum, say that "the greater curvature should be freed beyond the entrance of the short gastric vessels along the gastro lienal ligament, and the lesser curve freed as far as the œsophagus Unless this is done the tube cannot be constructed" The present case *suggests that for certain* patients this may be very dangerous advice

Experimental work in dogs indicates that there are well-defined limits to the devascularisation which the stomach will tolerate Le Veen (1948) found that total ligation of the main vessels in 30 dogs led to diffuse infection of the stomach wall in 4, and to the development of ulcers, presumably ischæmic in origin, on the greater curvature in 6 others Layne and Bergh (1943) found that ligation of *all four main arteries* caused gangrene of the middle two thirds of the stomach The most detailed study is that of Bernheim (1932), who showed that either the lesser curvature or the greater curvature may be totally devascularised without ill effect, as may the whole of one curvature and part of the other, but if *all* vessels are tied, gangrene develops—and when this develops it is always on the greater curvature

The only references I have found to the possibility of ig in surgical procedures in man are both over twenty years old Barber (1933) suggested that "abnormal stomachs and in individuals with impe circulation and poor neuro muscular tone," too devascularisation may lead to necrosis and Sm (1931) wrote "perforation may occur as a result impaired blood supply, and its frequency is in relation with the level of resection In high resectio wide berth must be given to the remaining blood s on the greater curvature" In no modern article resection which I have read is this danger empha or, indeed, mentioned

Probably in the ordinary standardised gastre for duodenal or lesser curve ulcer, there is no dange ischæmic necrosis But in elderly patients with genera arteriosclerosis, and especially in high resections highly placed ulcer requiring the construction of a of greater curvature for anastomosis, the danger may real In such cases the blood supply to this greater curvature should be carefully considered, at least the uppermost vas breve should be jea safeguarded, even at the expense of free mobilisa avoid this disaster, which is virtually irreparable

I have to thank the chief medical officer, Ministry of for permission to publish this report

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HUMIDIFICATION IN POSITIVE-PRESS RESPIRATION FOR BULBOSPINAL PARALYSIS

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The use of positive-pressure respiration tracheal tube in the treatment of bulbospinal requires adequate humidification of the air or gas need was emphasised by Lassen (1953) from his in the 1952 epidemic of poliomyelitis in Cop "a good humidifier is essential, otherwise secretion may occur" We describe here a which has proved itself satisfactory in clinical use open-circuit positive pressure system and can used in a closed-circuit system

The minimum level of humidification necessa avoid incrustation of secretions is uncertain, seems reasonable to reproduce as far as possible conditions existing in normal man when br through the nose

Perwitzschky (1927), in a most careful study, that when room air 40% saturated at 25°C was through the nose, the relative humidity in the lowe of the trachea was 98% and the temperature When the air was inhaled through a tracheotomy however, the relative humidity in the trachea was 51% These findings suggest that the aim in pressure respiration should be to deliver air throu tracheal tube at 36°C and 100% relative humidity

The technical requirements of positive pressure tors impose limitations on the methods of ilable. If positive pressure pumps such as the ıver (1953) respirator and the Radcliffe respiration nps A and B (Russell and Schuster 1953) are used l the humidifier is placed on the inspiratory side the pump cooling in the pump leads to condensation hin it and to eventual failure. Hence the humidifier st be placed between the pump and the patient is means that the humidifier must have a low resistance he desirable safety precaution of the pump working a low pressure is to be maintained In addition the midifier must be safe for the patient, require very le attention and be simple and cheap in design th these considerations in mind we experimented with eral methods of humidifying air and oxygen

Methods

To test the efficiency of various methods of humidifica n, wet bulb and dry bulb thermometers were placed a small well lagged glass jar through which air mped through the humidifier was led through rugated breathing tubing 3 ft long and lagged with ton wool 2 cm thick There was free exit from the so that the wet and dry bulbs were in a moving eam of air

Observations

sing Air Through Water

The first method to be tested was the time honoured of bubbling gas through water A common practice o bubble through about 4 cm of water in a Woulfe s tle at room temperature, but experiment shows that bbling air through as much as 15 cm of water at 46 C l humidify 3 litres of air per minute to the extent of y 87% The high resistance of this method and the ure to achieve 100% humidity led to its being ndoned

sing Air Through Wet Gauze

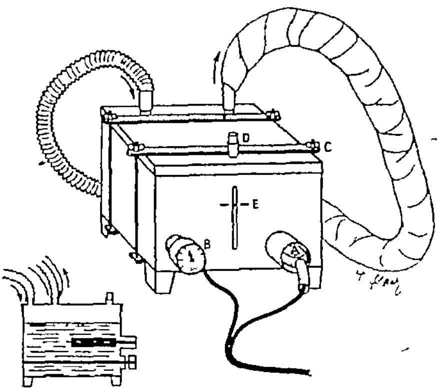
The next method in common use which was tested to pass the air through wet gauze Six litres of a minute were passed through a closed box across ich hung four curtains of wet gauze, each 12 cm are, the lower ends being in water at 41 C This thod achieved a relative humidity of only 70% 37°C

sing Air Over Warm Water

xford vaporiser—Wislicki (1953) recommended the of the Oxford Vaporiser as a combined inflator midifier for positive-pressure respiration Used in way the bellows draw air over water contained in ether chamber and pass it to the patient The mp is thus between the humidifier and the patient, ich is contrary to the principle mentioned above the method was given a trial. When the water ect of the vaporiser was heated to the maximum ording to the normal procedure and the ether con ler filled with water at an initial temperature of 90°C air was 100% humidified but its temperature could be maintained above 22 C This was due to the t degree of cooling taking place in the bellows. at 22 C is too cold for direct injection into the trachea, moreover air which is saturated at 22 C is only % saturated when warmed to 36°C

ew apparatus—Another apparatus (see figure) then built incorporating the same principle of passing over warm water but placing the pump before the midifier

his consisted of a water bath heated with an electrical ter (A) and controlled by a thermostat (B) The bath an airtight lid capable of withstanding an intermittent sure of 30 cm. of water The bath was rigid, and its was secured with clamps (C) compressing a gasket Air led into and out of the bath through two ⁷/₈ in brass es passing vertically through the lid and joined to lengths of corrugated breathing tubing A third brass tube (D) in the lid, occluded with a rubber bung was provided for filling the bath, and a window (E) in the side enabled the water level to be observed The level was such that there was about 5·5 litres of air above the water and the area of water over which the gas passed was 900 sq cm.



The apparatus: A plug of electric heater; B thermostat C, clamp; D water inlet; E window

This apparatus was tested both experimentally and clinically Experimentally air at 100% relative humidity could be delivered at temperatures up to 49°C which was the highest temperature tested When used clinically with the thermostat set at 50°C the air, after passage through a tube lagged with 2 cm of cotton wool and through the connections to the tracheotomy tube including an automatic spill valve, had a temperature of 35°C and a saturation of 100% The precise adjustment of the thermostat depends on the efficiency of the lagging of the breathing tube and the amount of heat lost in the connections to the tracheal tube before the air reaches the patient.

The influence of variations in the minute volume on the temperature and saturation of the delivered air was explored The results are given in the accompanying table from which it can be seen that these variations produced negligible changes in the temperature of the air until the minute volume was reduced to 3500 ml which is about half the minute-volume of the normal resting adult This is of considerable practical importance because once the thermostat was set for a certain delivery tube and connection no further adjustment was necessary when the stroke or minute volume was altered to the needs of the patient Likewise no adjustment was required when changing from room air to 100% oxygen

The only attention the apparatus required was the addition of a little water every twelve hours The use of a spring loaded plug for the heater obviated any danger from switching on the heater with the

EFFECT OF VARIATIONS IN MINUTE VOLUME ON TEMPERATURE AND HUMIDIFICATION OF AIR

Min. vol. (ml.)	Stroke vol (ml.)	Rate per min.	Temp. of thermostat (C)	Temp of air (°C)	Humidity (%)
20,000	1000	20	49	34 5	100
12 000	500	24	49	34 5	100
10,000	500	20	49	35 0	[illegible]
7000	500	14	49	34 5	[illegible]
3500	250	14	49	33·0	[illegible]

humidifier empty There was no danger of the water being inhaled, because the outlet tube went vertically through the lid of the water-bath and was well above the water level Since the humidifier stood on the floor and the breathing-tubing led up to the patient's bed, there was no possibility of spill, and water condensed in the tube ran back to the humidifier The resistance of this apparatus when transmitting 20 litres a minute in fifteen strokes was less than 3 cm of water Cultures of the air after its passage through the humidifier showed that it introduced no pathogens

In practice a humidifier of this size (30 cm square) was not inconveniently bulky The size can, however, be reduced by connecting the inlet and outlet tubes within the humidifier with a tube of sponge rubber 45 cm long and 2 cm internal diameter This can be made by sewing together the edges of a strip of 'Dunlopillo' 1 cm thick The sponge-rubber dips in the water and, when saturated, provides an adequate surface for vaporisation

Discussion

These observations emphasise the importance of measuring the effectiveness of clinical methods of humidification before putting them into use Though the time honoured methods of bubbling gas through water, or passing it through wet gauze, add some moisture, they are entirely inadequate if 100% humidification is desired In the present state of knowledge it seems reasonable to reproduce as closely as possible the conditions known to obtain in normal man, since the dangers of incrustation due to drying are well established and serious

The humidifier and heater described here is well suited for positive-pressure respiration It will humidify air or pure oxygen up to 100% saturation at a wide temperature range around body-temperature, it will deal with 20 litres of gas per minute, which is well in excess of normal requirements, and it does not require adjustment for changes in minute-volume The resistance of the apparatus is low, and the attention it requires minimal

This apparatus has had a thorough clinical trial, it has been used for four weeks for a patient on positive pressure respiration with satisfaction The secretions were always moist and could easily be removed from the trachea by suction through a fine catheter Viscid tenacious mucus and dry crusting in the trachea were not observed The patient appreciated the machine's action because, when it was removed from the circuit, she complained of discomfort

This simple piece of apparatus can be made in any hospital workshop at low cost, and can be recommended for extensive clinical use

Summary

Several commonly used methods of humidifying gas were found to be unsuitable for clinical use if 100% humidification is desired

An easily made apparatus is described which will humidify gas to 100% saturation at body-temperature, and can be used in positive pressure respiration

We wish to thank Dr W Ritchie Russell and Dr A Crampton Smith for their encouragement with this work, and Dr H G Epstein, of the Nuffield department of anæsthetics in the University of Oxford, for his advice One of us (J M) was in receipt of a grant from the Medical Research Council

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Preliminary Communication

EFFECT OF AN ANTI-THYROXINE COMPOUND ON THE METABOLISM OF RADIOACTIVE THYROXINE AND TRIIODOTHYRONINE IN RATS

IN previous communications (Maclagan, Sprott, Wilkinson 1952, Maclagan and Wilkinson 1952) it been suggested that the anti-thyroxine compound, 4 hydroxy 3 5 diiodobenzoate (B.H D B) owes its i bitory effect to interference with the deiodination thyroxine to triiodothyronine, the latter probably r senting the metabolically active form of the th hormone (Gross and Pitt Rivers 1952, 1953, Gross Rivers, and Trotter 1952) The enhancement of the of triiodothyronine by simultaneous treatment B H D B may also be explained on this assumption, if triiodothyronine is further deiodinated to p inactive substances, then interference with this p would increase its metabolic effects

In order to test this hypothesis, the urinary iodi rats treated with thyroxine labelled in the 3' 5' pos with ^{131}I was compared with that of animals B H D B in addition to similar doses of labelled th Two groups of 3 rats, each weighing 230 ± 20 g given oral suspensions of B H.D.B (50 mg per ml pe in 1% aqueous carbomethoxycellulose on the first 25 mg per 0 5 ml per rat on each succeeding day experiment Two further groups of 3 rats received medium only On the second day the rats in all groups each received a single subcutaneous inje the thyroxine solution (0 5 ml 0 02N Na_2CO_3 100 µg , 67 µc thyroxine per rat) Each group placed in a metabolism cage and the urine and collected daily After suitable dilution, the radioa in each was measured and the results expressed a percentage of the dose administered

TABLE I—EFFECT OF B H D B ON URINARY IODIDE OF R TREATED WITH THYROXINE

Groups of 3 rats treated with	Percentage of dose excreted after	
	48 hours	120 h
Thyroxine (4 µg /rat)	11 8 16 7	[illegible] [illegible]
Thyroxine (4 µg /rat) + B.H D.B *	6 1 4 8	[illegible] [illegible]
Thyroxine (100 µg /rat)	12 5 12 4	[illegible] [illegible]
Thyroxine (100 µg /rat) + B H.D.B *	3 2 3·0	[illegible] [illegible]

* See text for dosage of B.H D.B

TABLE II—EFFECT OF B.H.D.B ON URINARY IODIDE OF TREATED WITH TRIIODOTHYRONINE

Groups of 3 rats treated with	Percentage of dose excreted after	
	48 hours	[illegible]
Triiodothyronine (6 µg /rat)	21 3 20 7	[illegible] [illegible]
Triiodothyronine (6 µg /rat) + B H.D B *	5 2 9 4	[illegible] [illegible]
Triiodothyronine (30 µg /rat)	18 4 31·6	[illegible] [illegible]
Triiodothyronine (30 µg /rat) + B.H D.B.*	6 3 8·0	[illegible] [illegible]

* See text for dosage of B H.D B

A similar experiment in which 4 µg doses of thyroxine ere given was also performed The results of both xperiments appear in table I

Further experiments in which triiodothyronine labelled n the 3 position with ^{131}I was given in doses of 6 µg nd 30 µg per rat in place of thyroxine were also carried ut The results of these are summarised in table II

It is clear that when given simultaneously with hyroxine or triiodothyronine B.H.D.B reduces the xcretion of urinary iodide in intact rats. Thus support given to the hypothesis that it owes its action to terference with processes of deiodination of these two omponents of thyroid secretion.

Part of this work has been briefly described (Wilkinson nd Maclagan 1953) and a fuller report will appear ewhere (Wilkinson et al 1953) These results in tact rats are at variance with those of Roche Deltour, nd Michel (1953) who found that in thyroidectomised ts B.H.D.B actually increases the rate of deiodination f thyroxine labelled in the 3′:5′ positions with ^{131}I It ould be premature to discuss the cause of this apparent ontradiction, but it seems that the mode of action of B.H.D.B may be entirely different in intact and thyroidectomised rats

The radioactive thyroxine was obtained from the Radiochemical Centre Amersham, and the radio triiodothyronine was prepared from 3:5-diiodothyronine kindly provided by Glaxo Laboratories Ltd.

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Reviews of Books

iuretic Therapy

Pharmacology of Diuretic Agents and Clinical Management of the Edematous Patient ALFRED VOGL, M.D assistant professor of clinical medicine New York University College of Medicine Baltimore: Williams & Wilkins London: Baillière Tindall & Cox 1953 Pp 248 38s 6d

THOUGH the title of this book may suggest another llestone in the fragmentation of treatment such mis vings are dispelled by A. M Fishberg's foreword, and en more by the actual contents of the book. It is up-to-date balanced and comprehensive review of e methods of relieving oedema

Specific treatment of the underlying disease when available mentioned in outline only; but there is a detailed and ctical account not only of diuretic agents but also of the tionale and effects of low salt diets and cation exchange ins. There are short introductory chapters on the causes oedema, and the pharmacology of diuretic agents but o-thirds of the book is devoted to the practical management oedema. As might be expected of the discoverer of the uretic action of organic mercurials, these are fully dealt th, and there is perhaps no better account available of the arious causes of mercury fastness. The indications for pplementing mercurial diuresis with aminophylline exchange ins, and decholin are considered in detail. In view of the neral high quality of the book, it is surprising to find no ention of carbonic anhydrase inhibitors as diuretics, though lphonamide compounds have been used in this way for me years; a few of the details of treatment reflect American etary habits and facilities.

Most cardiologists and general physicians would find ch in this book to interest them There is a biblio aphy of 725 references not all American

troduction to Functional Histology

GEOFFREY BOURNE, D.SC D.PHIL. reader in histology London Hospital Medical College London: J & A Churchill 1953 Pp 108 21s

Dr Bourne does not set out to provide a textbook of stology but rather to supplement existing books with account which emphasises the functional, rather than e structural, features of cells and tissues. He has ceeded well in his purpose and a wide reading public students medical practitioners, and investigators will grateful to him His accounts are concise and informa ve they are also readable—indeed vivid—so that they splay the complex machinery of the living cell as a ghly organised factory of enzyme operatives, while the ochemistry of the simultaneous cell processes of kata lism synthesis, and respiration are clearly explained he 98 illustrations are carefully selected and instructive: many of them are electron microscope photographs. At the end of the book there is a useful chapter on the more recent histochemical techniques.

Atlas of Tumor Pathology

Fascicle 14: Tumors of the Thyroid Gland. SHIELDS WARREN M.D., professor of pathology and WILLIAM A MEISSNER M.D assistant professor of pathology Harvard Medical School 1953 Pp 97 $1.75

Fascicle 15: Tumors of the Parathyroid Glands BENJAMIN CASTLEMAN M.D acting chief department of pathology and bacteriology Massachusetts General Hospital 1952 Pp 74 65 cents.

Fascicle 17 Tumors of the Lower Respiratory Tract AVERILL A. LIEBOW M.D professor of pathology Yale University School of Medicine 1952. Pp 189 $1.25

Washington, D.C.: Armed Forces Institute of Pathology

Fascicle 14—Dr Warren and Dr Meissner refer to misunderstanding and confusion in classification and in views about the evolution and especially evaluation of thyroid tumours. The opinions of both pathologists and clinicians range from "enthusiastic overestimation to regrettable underestimation" of their potentialities.

The growth habits of these tumours differ from those of other tumours in several respects, for they are subject to variation and even to apparent inconsistencies The authors find that a true follicular adenoma produces symptoms of clinical hyperthyroidism in only about 1% of cases for Graves's disease is usually associated with a nodule showing excessive hyperplasia in an adenomatous goitre Clinical distinction between an adenoma and a carcinoma may be difficult, for surgeons estimates of the incidence of carcinoma in discrete nodules in the gland run as high as 20%. When studied pathologically some of these thyroids will turn out to have adenomatous goitre with multiple nodules. Nevertheless Dr Warren and Dr Meissner say surgical excision is the proper treatment because cancerous change in adenomas may be common. The giant-cell and follicular cancers in particular suggest transition from a follicular adenoma. In the papillary carcinomas, which are commoner evidence of transition is less striking but it is suggested that most of them may be malignant from their inception. Proof is lacking that the hyperplasia seen in Graves's disease sometimes leads to cancer and no increase of cancer seems to be resulting from the hyperplasia induced by thiouracil

This important survey is based on the clinicopathological study of 600 cases of carcinoma of the thyroid and several thousand benign tumours

Fascicle 15—Dr Castleman in his admirable and exhaustive account of the pathology of the parathyroid glands reviews 100 cases of primary hyperparathyroidism from the records of the Massachusetts General Hospital An adenoma was present in 89 of them, the lower glands being involved thrice as often as the upper—whereas in primary hyperparathyroidism not associated with tumour formation it is usually the upper glands which show the greater degree of hypertrophy A fifth of the adenomas were mediastinal Dr Castleman subscribes to the view that recurrences after operation are due to the original invasiveness of the tumour rather than to any accidental spilling of adenoma tissue at operation Although malignancy is rare, the histological assessment of a parathyroid tumour requires to be made with care

The illustrations, conforming to the high level of previous fascicles, include an instructive set of photomicrographs of serial tibial biopsies in a case of osteitis fibrosa cystica taken before and after operation

Fascicle 17 —Dr Liebow gives a full account of tumours of the lower respiratory-tract and pays special attention to what is seen through the bronchoscope and at operation He discusses atypical proliferation but doubts whether carcinoma often develops as a result of metaplasia An illustration of atypical epithelium is included, which, in preparations of sputum, would surely raise the suspicion of carcinoma. Dr Liebow supports the view that adenomas, comprising 6–8% of lung tumours, are derived from the mucus-secreting glands and their ducts Metastases may occur, but they are "rare, sluggish and usually inconsequential" The cylindroid variety seems to show greater invasiveness than the carcinoid

This fascicle includes a useful illustrated account of malignant cells in sputum and in pleural fluids

Slipped Capital Femoral Epiphysis

ARMIN KLEIN, M D, ROBERT J JOPLIN, M D, JOHN A REIDY, M D, JOSEPH HANELIN, M D, Massachusetts General Hospital, Boston Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1953 Pp 130 49*s*

THIS short monograph is one of the American Lectures in Roentgen Diagnosis series and naturally emphasises early diagnosis of the condition The text is brief and clear, following, in the main, the same lines as most orthopædic teaching in Great Britain It offers no new ideas, and has nothing to say about ætiology, but it lays down clear criteria on which the diagnosis should be made The radiographs are outstandingly good, most are reproduced without any reduction, and there is a splendid series of films showing the normal male and female hip from the age of a week to 17 years

In the section on treatment the authors recommend early weight bearing after fixation, even in cases needing open reduction This they reserve for cases with a slip of more than 1 cm, and of such duration that closed reduction is impossible, a Smith Petersen nail is used in all cases, and they recommend its later removal, to avoid the not uncommon complication of fracture of the femoral shaft at the site of the pin head They illustrate several cases where growth has continued for several years after pinning, so that the pin was left behind and no longer penetrated the epiphyseal plate They apparently find no need for any wedge resection of the metaphysis of the neck, as used by Foley in this country to get rid of the new formed bone, nor do they mention the possible danger of stretching the posterior capsular vessels over the "beak" at the back of the neck if reduction is done without this precaution Nevertheless, in their series of 81 cases, they do not seem to have had any examples of aseptic necrosis of the femoral head Suitable warnings are given about the danger of the contralateral hip slipping, even when the patient is laid up in bed

This little book will be welcome to both radiologists and orthopædic surgeons

Treasury of Human Inheritance

Vol 5 Part 2 *On Syndactyly and its Association with Polydactyly* JULIA BELL M A, F R C P London Cambridge University Press 1953 Pp 50 10*s* 6*d*

DR Bell has once again done a valuable service to students of human heredity by collecting and analysing all the published pedigrees of one group of abnormalities The deformity here considered is essentially syndactyly Polydactyly is included only where it is associated with syndactyly and syndactyly is the predominant deformity Pedigrees where polydactyly is the outstanding deformity are to be considered in another volume

There are many varieties of syndactyly (the great maj of them occur sporadically) Dr Bell has, however, been a to separate the 63 published pedigrees into two main gro leaving a relatively small unclassifiable residue The lar group are those in which there is webbing of the second third toes with no abnormality of the hands The ot common group is characterised by webbing of the ring middle fingers It is not unusual for the fourth finger to b part reduplicated and this reduplication is included in web It is rare to find webbing of the hands associated w webbing of the second and third toes (that is to say, a c tion of the features of the two main groups), but many of individuals with webbing of the ring and middle fingers webbing of the fourth and fifth toes, often with a reduplica little toe included in the web

There is one apparent instance of inheritance deter by the gene on the Y chromosome here there was bil webbing in 14 males in four generations and every son of affected male was also affected

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British Encyclopædia of Medical Practice (2nd London Butterworth 1953) *Pharmacopœia* (Pp 65*s*) and *Index* (Pp 386 65*s*) —These two volumes off the new edition of the encyclopædia, which is under general editorship of Lord Horder The pharmacopœia originally designed to deal with the proprietary p mentioned in the main text, but new substances have so quickly that its scope has been extended to include more promising newcomers The drugs are listed alphabeti by their proprietary names, and the book will thus be a help in discovering what lies behind these catchy but uninformative titles There are brief accounts of the chemist pharmacology, uses, and side effects of each drug, and particularly useful to be able to look up the different quanti and packs in which the preparations are put out by the ma facturers (we hope it will not be long before a small num of standard packings are introduced to bring some order the present bewildering range) The index, compiled Mr J K Burgess, supplements the individual indices in volume by drawing together all the references to a p subject throughout the encyclopædia Finally, the pub of two further progress volumes, *Cumulative Supplement* (Pp 140 25*s*) and *Medical Progress 1953* (Pp 358 3 (the two together cost 52*s* 6*d*), brings the whole work up to date

Rawling's Landmarks and Surface Markings Human Body (9th ed London H K Lewis 1953 Pp 12*s* 6*d*) —Most things in medicine change, but evolut so stately a process that the outlines of our inner o our surfaces remain, thank heaven, much the same Th small comfort to the new generations of students who ha master them, and to whom—unless they see themselves future surgeons—surface markings remain an ins sible bit of flim flam tacked on by the examiners to an al overloaded curriculum But this rebellion is dumb and as they approach the crucial moment they rhythmically to "Rawlings," like their fathers before th and there it all is How happy is Mr J O Robinso present editor, compared with those invited to revise bacteriology, vitamins, the endocrine system, or other topics All he had to do, the publishers tell us in a note to make a few minor alterations in the text, these bei that were thought necessary The section on ossification epiphyses of the skeleton has been extended, however embellished with several new illustrations This is a val twelve and sixpennyworth

Diseases of Women (9th ed London Edward 1953 Pp 480 28*s*) —The last edition of "Ten Teache appeared four years ago under the editorship of Mr C White, Mr Frank Cook, and Sir William Gilliatt The editorial triad—Mr Frederick Roques, Mr John Beattie, Mr Joseph Wrigley—have had four of the former contributors to help them as well as three newcomers, the principle of sharing the responsibility for the book tively has been maintained Individual contributors, how have been allowed rather more scope than in former edit in the hope that they would be rather more downright dogmatic than their forerunners, but equally orth Students demand from their teachers both these which fortunately are not mutually exclusive and it as though this new edition exactly meets their re

THE LANCET

LONDON SATURDAY, NOV 14 1953

Hypothermia

In the past few years the deliberate induction of hypothermia has come to the fore as a means of lessening certain operative and anæsthetic risks Reduction of body temperature, and therefore of metabolism cuts down the oxygen needs of highly specialised organs such as the brain and heart to the level of less important tissues and the blood-supply to these organs can then be temporarily interrupted or diminished There are, however, dangers in hypothermic states and a considerable amount of experimental work has been carried out in attempts to assess the various factors concerned

In this issue Dr Churchill-Davidson and his colleagues describe experiments on surface cooling by immersion in iced water designed to assess the dangers of this technique Their results in dogs, which do not differ greatly from those previously reported, suggest that surface cooling is a simple and safe method of reducing the body temperature, provided this is not allowed to fall below 26°C Clinically, this method is likely to be restricted to children while cooling of the blood stream by means of the extracorporeal circulation, as described by Delorme[1] may be preferable for adults. Special blankets through which ice cold water is circulated in pipes and on which the patient lies, is an alternative With this method skin necrosis may very occasionally ensue owing to the uneven pressure of the dependent parts of the body on the blanket, but this slight risk has to be set against the physiological disadvantages of the extracorporeal circulation with the associated need to insert a cannula into a large artery and vein All these methods produce an effect only slowly—upwards of four hours may be needed to bring a normal sized adult to a temperature of 26°C—and cooling of the peritoneal or the pleural cavity which is mentioned by Churchill-Davidson and his colleagues, certainly warrants further trial These investigators have clearly shown the dangers, first of ventricular fibrillation at temperatures below 26°C, and secondly of unexplained fatal pulmonary complications after rewarming Cardiac arrhythmias are usual below 5°C, and occasionally ventricular fibrillation develops which is irreversible at temperatures below 22°C This work has been done on normal dogs in which the margin of safety was found to decrease with increasing age The most obvious clinical application of hypothermia is in the operative treatment of congenital heart-disease in children but though young these patients have far from normal hearts, and the complications of cooling might easily arise at higher temperatures than those found experimentally to be safe Further experimental work will no doubt be directed to averting these dangerous complications, since there is little doubt that hypothermia is of practical value One reason why it has been developed is in order to work safely in a dry heart, and this ideal will not be achieved solely with hypothermia, except for brief periods unless very low temperatures can be obtained

In the light of our present knowledge there is little or no justification for using this technique for surgical operations which can be properly done without its aid In cardiac surgery the clearest occasions for its use seem to be for operations on the great vessels which cannot be completed without temporarily stopping the blood supply to a vital organ such as the brain, and for operations to repair septal defects in the heart Lewis and Taufic[2] have already reported the closure of an atrial defect with the aid of hypothermia in a girl aged 5 years who recovered fully and other workers have had similar successes but the dangers of the operation are considerable Unless the cardiac outflow is occluded low enough to include the origin of the coronary arteries, air may enter these during the opening of the heart, and even if this is avoided ventricular fibrillation is always likely

Hypothermia has been used clinically as an ancillary to the surgical treatment of the tetrad of Fallot by the Blalock Taussig operation This would as yet hardly seem an acceptable indication the operation has been done without hypothermia in many thousands of cases with so low an immediate mortality as to suggest that in most cases reduction of body temperature may enhance rather than decrease the risk Moreover the fall of pressure in the right ventricle that accompanies the general fall of blood pressure when the body is cooled may prove disadvantageous—and even dangerous—in the presence of obstruction at the pulmonary valve In very severe cases, where a high operative mortality is to be expected, there may be some justification for cooling, but the wish to assess the practical value of this new method should not obscure the possibility that there is no real need for it Hypothermia may prove useful in neurosurgery and in a limited form, in cases needing anæsthesia with controlled hypotension since some of the hazards of hypotension could be diminished by decreasing the oxygen needs A moderate reduction of temperature may become a valuable adjunct to the use of the artificial heart It may also be of value in the treatment of shock, and in toxic illnesses in which fever is prominent and the normal defensive mechanism of the body inadequate

In some Continental clinics various agents are given before during and after operation to lower metabolism by producing a state of artificial hibernation[3,4] and French work in this connection is reviewed by a correspondent on a later page Hypothermia is often used as an ancillary to this method—in fact many of the drugs prescribed facilitate cooling by depressing the temperature regulating mechanisms—though irrespective of deliberate cooling the body temperature will fall a degree or so Much of the success of the technique apparently depends on chlorpromazine hydrochloride ('Largactil'), which has been developed from compounds of the anti-histamine group, though it is almost devoid itself of anti histamine activity This drug is said to depress various parts of the autonomic and central nervous systems, and also the endocrine system The patient will gain great advantage if it proves possible to depress differentially the body-readjustments that follow the trauma of surgery and anæsthesia, so that harmful processes are retarded and reparative ones allowed to progress

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[1] Delorme E J *Lancet* 1952 ii 914

[2] Lewis, F J., Taufic, M. *Surgery* 1953 33, 52.

[3] Laborit H., Huguenard P *Pr méd* 1951 59 1329

[4] Huguenard P *Anesth. Analg* 1953 10 10.

Many problems concerning hypothermia are still unsolved, and meanwhile its clinical application should be confined to patients whom it is clearly likely to benefit

Subclinical Poliomyelitis Infections

EPIDEMIOLOGISTS concerned with the prevention of poliomyelitis need to know how many silent subclinical cases accompany each overt paralytic infection Estimates, based on indirect methods, have varied from 100 to 1000 subclinical infections to each paralytic case Thus, MELNICK [1] measured the amount of virus excreted into New York sewage at a time when the incidence of poliomyelitis was low, and he concluded that there were about 1000 silent excretors of virus to each paralytic case COLLINS [2] found that only about 1% of young adults aged 20–24 gave a history of paralytic poliomyelitis, and since the attack-rates are negligible above this age he concluded that adult immunity had been gained at a cost of 1 paralytic illness to about 100 abortive infections HOWE [3] compared attack-rates of measles and poliomyelitis, and by reasoning similar to that of COLLINS he concluded that there were about 200 subclinical infections to each paralytic case Many epidemiologists, however, regard these figures as excessive Thus, BRADLEY [4] speaks of "the probability that the infection moves through a relatively narrow stream of the population", and AGERHOLM,[5] taking up this idea, suggests that damming the stream might halt the flow of the disease and should not prove too difficult administratively

MELNICK and LEDINKO [6] have now found strong evidence against the hypothesis of a narrow stream of infection. These workers used the new tissue-culture techniques for studying neutralising antibodies to the poliomyelitis viruses They investigated samples of serum from 200 children in Winston-Salem, North Carolina, who were bled in 1948, first just before a poliomyelitis epidemic and again six months afterwards Tests of the pre epidemic sera revealed a very low previous incidence of infection with any of the three types of poliomyelitis virus in children under 4 years of age, but a higher proportion of older children showed antibodies—a finding which correlated well with the fact that the last outbreak of poliomyelitis before that of 1948 was in 1944 Sera taken after the 1948 epidemic showed that quite a high proportion of children had developed antibody to poliomyelitis viruses of types 1 and 2 during the summer, no evidence was found of infection with type-3 virus MELNICK and LEDINKO calculated the proportions of children in different age groups infected during the epidemic They infection-rates were then compared with the known paralysis-rates in the epidemic, and it was found that the number of subclinical infections per paralytic case was 175 for infants under 1 year of age, 100 for children aged 1–2 years, 73 for children aged 3–4 years, 62 for children aged 5–9 years, and 95 for children aged 10–14 years It was also found that previous infection with virus of type 2 or 3 did not prevent infection with type-1 virus in 1948 MELNICK and LEDINKO did not investigate whether adults were undergoing subclinical infections during the epidemic, and this may be an additional source of spread.

These findings suggest that poliomyelitis cannot be accurately pictured as moving in narrow streams through the community, and that the major part of the flow is through wide, subterranean channels Quarantine restrictions against poliomyelitis have been likened to closing the stable door after the horse has bolted They are better compared to mending a leaking bottle after most of its noxious contents have already escaped, the attempt to prevent the last few drops from escaping, however desirable, should be viewed in the light of the damage already done This new evidence will discourage the adoption of stricter quarantine measures The main hope at present is from vaccines[7], but because of the large number of subclinical infections and the low paralytic rates, it may prove difficult to assess their protective power The aim will be to produce either a live attenuated virus vaccine which will confer lifelong immunity, or else a killed virus vaccine which will convert the paralytic cases into silent subclinical infections

Diarrhœa after Gastrectomy

A NOT uncommon consequence of gastrectomy is looseness of the bowels, sometimes amounting to diarrhœa, starting two or three days after the operation Though usually transient this may last for weeks or even months It has usually been attributed to the greatly diminished secretion of hydrochloric acid in the days immediately after the operation, and the neutralisation of any acid present by the pancreatic and intestinal juices which now have free access to the cavity of the stomach remnant Ingested bacteria, no longer destroyed by the acid, pass into the jejunum where they find conditions eminently suitable for propagation The upper part of the small intestine reacts by becoming inflamed and pouring out large quantities of exudate How exactly accommodation to the strange new state of affairs takes place we do not know On an earlier page Dr WILLIAMS and Mr PULLAN describe the illness of the patients in whom the diarrhœa was so severe as to cause death in five and to threaten life in the remainder Fortunately the condition can rarely be as serious as this, for they could find only these ten cases in all the St Thomas's Hospital records The patients present a characteristic picture The operation proceeds as usual, and for forty-eight hours all s to be well Then diarrhœa sets in, and with it com latory collapse so great that within two or three da the patient may die The pulse is rapid and threa

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1 Melnick J L *Amer J Hyg* 1947 45 240
2 Collins S D *Publ Hlth Rep Wash* 1946 61 327
3 Howe H A *In* Viral and Rickettsial Diseases of Man Edited by T M RIVERS Philadelphia 1952
4 Bradley W H Papers and Discussions of 2nd International Conference on Poliomyelitis Philadelphia and London 1952
5 Agerholm M *Lancet* Aug 8 1953 p 287
6 [illegible], J L Ledinko N *Amer J Hyg* 1953 58 207

7 See *Lancet*, 1953, i, 777

d the blood pressure is too low to record, the nperature is usually raised There are no signs of :itonitis, but there are cyanosis, a pinched face d dyspnœa The intensity of the collapse seems to related to the enormous amount of liquid lost by the wel If the patient dies, necropsy shows extensive crosis of the mucosa *of the small intestine a large* bular slough may form Microscopically there is tle cellular infiltration, and the submucosa is intact, if the patient recovers regeneration can take place om the deeper parts of the glands No abnormality n be seen in radiographs subsequently taken after a rium meal The stomach shows no abnormal anges, and repair at the suture lines appears to be ing on satisfactorily Recovery is quite rapid if ergetic measures are taken These consist in the fusion of glucose saline solution in large quantities—metimes as much as three litres an hour during the utest stages It seems also essential to replace otein loss by plasma or whole blood

The cause of this serious complication is not clear *o significant alteration in the intestinal flora could be* und by WILLIAMS and PULLAN *Clostridium welchii* not mentioned as being present, though it must be esumed that anaerobic cultures were made Some ght may be thrown on this problem by the observa ons made by Professor HOWIE and his colleagues lso in this issue), who found *Cl welchii* in the pirated gastric contents in twelve of fifteen patients bmitted to gastrectomy of whom only one had a tle diarrhœa The presence of toxin in the aspirated quid suggests that the *Cl welchii* were not just in ansit but were living in the stomach. The patients rum was found to contain only negligible amounts of ititoxin but no great importance should be attached this observation since the serum of a woman with *ere Cl welchii* postpartum *infection contained only* ry small amounts The suggestion is that the wering of the acidity in the stomach after gastrec my allows the organism to survive within it, and e alkaline anaerobic conditions of the jejunum are ry favourable to its growth. The absence of flammatory reaction in the deeper part of the wall the intestine gainsays invasion of this by the ganism The diarrhœa could be ultimately a emical irritation due to the toxin amounting to rosion of the superficial layer of the bowel wall

W WILLIAMS in 1927 pointed out, in an important iper on the toxæmia of intestinal obstruction[1] that *welchii* could not flourish in the small intestine cause of the rapid passage of food through it and e acid in the large intestine was apt to kill it off so at on culture of the fæces, it could not be demons ated Yet it seems almost inconceivable that with e intense diarrhœa of the very severe cases now ported by WILLIAMS and PULLAN there should be evidence of its presence in the fæces

In another paper this week Mr RUTTER records a se in which necrosis of the gastric remnant developed ter subtotal gastrectomy *Bacteriological findings* e not recorded, but it seems possible that infection th *Cl. welchii* contributed to the patient s death. he next step will be to find out whether antitoxin effective in such cases as are reported in these three ticles or is even indicated as a prophylactic before peration

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[1] *Lancet* 1927 i 907

Annotations

THE ASCENT OF EVEREST

A THRILL enhanced by its happy coincidence with the Coronation must have been felt by most people in Britain when the news resounded through the rain-swept and crowded streets on June 2 that Everest had at last been climbed Men and women who had never before admitted an interest in mountain climbing felt that something symbolic had happened.

Since the first attempt in 1921 doctors have played their part in many ways upon the mountain. But, like Dr Michael Ward in 1953 they have mostly gone as climbers or at any rate as experienced mountain travellers, with their medical responsibilities added to their primary duty of getting up the mountain or helping others to get there It is surprising, in the circumstances that they have found the time to bring back so much physiological material and so many new facts about the medical aspects of great altitudes now comfortably enshrined in standard textbooks of physiology The 1953 expedition differed from its predecessors in having with it a physio*logist who was not a mountaineer It would be unkind to* his distinguished predecessors to suggest that he was in consequence the better physiologist but no man can serve two masters when both are hard taskmasters. This time Dr L G Pugh was able to apply his whole mind to the physiological problems of life at great altitudes

The Ascent of Everest,[1] Sir John Hunt s account of the expedition, is published this week It is a remarkable work made the more noteworthy by beautiful photographs in colour the preparation of such a volume in so short a time is no mean feat. Appendices by Dr Pugh and Dr Ward suggest that full use was made of opportunities never before accorded to a professional physiologist The account of the physiological difficulties encountered is admirably clear and whets the appetite for the more detailed and technical reports which is presumably being prepared It is impossible in a book intended for the lay reader to do more than explain the general principles which are already well known to medical readers Pugh and Ward emphasise the importance long realised, of slow acclimatisation from 14 000 feet up to about 23 000 feet and of spending as short a time as possible above this level lest deterioration should set in, adding the new and interesting observation that men going too quickly to even 18 000 *feet suffer not merely from lack of acclimatisation but* from earlier deterioration. Like their predecessors in 1933 they found that tired and overstressed men recovered completely only if sent to lower levels The added work of a fresh ascent later was undertaken in better heart They confirmed too that old timers acclimatise more quickly than greenhorns in the Himalaya

Matters of diet fluid and electrolytes were neglected by pre-war expeditions—such things were not yet in the news. Members of the early expeditions were ill acclimatised and suffered from anorexia The 1933 expedition was well acclimatised and unprepared for the hearty appetites of its members. The expeditions of the later '30s were a little too much addicted to that toughness which as Pugh and Ward say has no place in Himalayan climbing Probably no Himalayan expedition has been as well fed as this one, but even *so there* were times when food ran short. Anorexia was proved to be a symptom of ill health and so of lack of acclimatisation and by inference of bad organisation. Cooking of an adequate diet at great altitudes was greatly improved by the use of pressure-cookers which were so successful that the Sherpas a conservative race went so far as to improvise their own pressure cooker out of old tin cans A low fluid intake has often been suspected of being a part cause of fatigue at great altitudes, where every drop of moisture must be obtained by melting snow—a process laborious and expensive in fuel and therefore in man-power Somehow or other the 1953 expedition managed to ensure an intake of 5–7 pints per man, compared with the single pint consumed by the Swiss in 1952 Since much of the fluid loss is by way of the lungs rather than the skin, loss of salt was a less serious problem and easier to solve

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[1] The Ascent of Everest. By Brigadier Sir JOHN HUNT C.B.E., D.S.O London: Hodder & Stoughton. Pp 300 25s

We shall look forward to a more detailed discussion of the oxygen problem That oxygen, given a suitable apparatus for its carriage, would be of inestimable benefit has never been doubted by serious physiologists Whether it is necessary is another and more difficult matter It has never been proved that man cannot reach the summit of Everest without it, and the arguments that he cannot which have lately been put forward (and rather mysteriously accepted without question) have been very specious Five men have reached 28,000 feet without oxygen apparatus, and it is doubtful whether any of them were turned back by oxygen deficiency alone That a ceiling exists is certain, but we are not yet sure that it lies below 29,000 feet This is one of the few puzzles which the 1953 expedition has left unsolved

PLASTIC SURGICAL DRESSINGS

IDEALLY a dressing should be protective against bacteria and abrasion, flexible but tough, transparent, and permeable to water vapour Furthermore it should be innocuous to tissue, it should not interfere with chemotherapeutic agents, and it should not be too costly

Flexible collodion forms a plastic, adhesive, and cheap dressing, but on evaporation of the solvent it contracts, and furthermore it hermetically seals the wound The various adhesive elastic dressings are either impermeable to moisture or irritating to skin, and they are opaque, while adhesive cellulose tape does not allow evaporation of sweat, although it has been used for some purposes—for example, strapping umbilical hernia in infants [1]

Farquhar and Lewis [2] suggested transparent 'Polythene' sheeting strapped over a window in a gauze swab as a dressing for transfusion wounds, so that the incision could be watched for sepsis without exposing it More recently a partially hydrolysed casein gel has been used in the treatment of burns [3] The dressing forms an insoluble protective film of coagulum which is pliable and also semipermeable, permitting evaporation of water, but it is not transparent Polyvinyl plastic [4] is being tested as a dressing which may be sprayed on burns from an aerosol can or pump On evaporation of the solvent, it forms a tough, flexible, adhesive, and transparent film which is permeable to water vapour but not to bacteria Experimental trials have been encouraging, but trials in man have not yet been reported

A plastic surgical dressing ('Bonoplast') described at the conference of Scandinavian surgeons in June has aroused much interest This substance is an acrylic resin dissolved in a mixture of acetic esters, and when spread thinly on the dry skin with a polythene applicator it forms in a matter of minutes a tough, transparent film which is permeable to moisture The film is not injurious to tissue, and experimentally superficial wounds have healed more cleanly than in a control series where conventional gauze dressings were used The solution is self sterilising, and the resultant film impervious to bacteria, surgeons have used it for preparing the operation field, making the incision through the dry film and then painting over the operative wound after sutures and clips are in position. The film eventually flakes at the margins and can be stripped from the removal being aided by spirit or benzene Disadvant are few One is that the film will not adhere to a surface The solvent is inflammable, but the dried is not and may be cut with the diathermy knife solvent gives rise to temporary stinging in unanæsthetis tissue, and there is a tendency for bleeding to be local prolonged, but this may be minimised by good stasis and suturing The dressing has much to it for certain fields—for example, herniotomies in —where the wound requires protection from local Because the dressing is pliable it may be used in region of joints, and it has also proved satisfactor facial work It seems not to antagonise the at the point of contact, and it has been suggested an antibiotic might be incorporated in it Finally, these days of rising costs, it is of particular interest Swedish hospitals carrying out trials have found a saving in the cost of surgical dressings—not to speak the very considerable economy in the nursing-time The preparation of an aerosol means expense, but the simple applicator gives perfe satisfactory results Further trials are taking place in Sweden and in the United Kingdom

ALCOHOLISM IN FRANCE

ACCORDING to a W H O report,[1] France in 1945 1420 alcoholics with complications per 100,000 (a prevalence exceeded only in Switzerland with and Chile with 1497), while the total number of F alcoholics, with and without complications, per 100 adults was 2850, which was exceeded only in the U.S. with 3952

Rouvillois and Dérobert [2] find that in the century there have been five well defined phases

1900 to 1914 —Alcoholism was rife, and the evils of a contributed to its steady rise without any legislative re

1914 to 1918 —Owing to the war, anti liquor laws passed The manufacture and sale of absinthe was pro in 1915, the number of licensed premises was reduced in and drunkenness was suppressed in 1917—which re in a decrease in alcoholism to a level lower than had obtained

1919 to 1939 —Legislation favouring the productio alcoholic drink was introduced as a result of pressure vested interests of the liquor trade the war time laws revoked and various new laws were introduced, such as of 1922 allowing the manufacture of alcoholic drinks with aniseed base, replacing the former absinthe, various permitting the re opening of licensed premises closed the war and the opening of new ones, and a law in giving exchequer aid to the advertisement of alcoholic During this phase alcoholism increased again, and by outbreak of the second world war had reached a higher than ever before

1939 to 1945 —Alcoholism increased by leaps and during the period of mobilisation, the "phoney" war, German invasion, but diminished during the years of occ tion, with its hardships and scarcities and repressive legislation At the time of the Liberation, alcoholism almost be said to be non-existent in France

1945 to 1952 —The experience of the two wars had impression on the legislature which, under pressure the liquor trade, repealed the restrictive anti liquor laws of Vichy régime and passed laws favouring expansion of trade Thus a law passed in January, 1950, perm the advertisement of liquor, another in March, 1951, allo the opening of licensed premises on aerodromes, and laws in the same year re-established the unrestricted manu ture and sale of alcoholic apéritifs, and the rebuilding licensed premises

Rouvillois and Dérobert base estimates of alcohol on three sets of figures deaths from cirrhosis of liver, deaths from delirium tremens, and admissions mental hospitals of patients with alcoholic psyc ho fluctuations in alcoholism as shown by these three gures agree closely with the trends of legislative control. eaths from delirium tremens per 100 000 population ere just under 3 in 1935 fell to less than 1 in 1944 nd from 1946 rose steadily to just over 6 in 1951 eaths from cirrhosis of the liver fell from about 16 per 00 000 in 1935 to about 7 in the war years, then rose harply to about 19 in 1951 Admissions to mental stitutions for alcoholic psychoses amounted to 8 per 00 000 in 1935–39, then fell to under 2 during the war, nd thereafter rose steeply to over 18 in 1951

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[1] Prince G E J Pediat 1951, 39 481
[2] Farquhar J W Lewis, I C Lancet, 1948, ii 244
[3] J Amer med Ass 1953 152 611
[4] Chou, D S J Went W E U S Forces med J 1952 3, 1241

[1] *Tech Rep Wld Hlth Org* 1951, no 42, p 20
[2] Rouvillois H Dérobert, L *Bull Acad Méd., Paris* 137 362

Rouvillois and Dérobert suggest that the continuing harp rise in all these figures is due to the laxity of the ws, and that the increase of alcoholism in France emands the urgent attention of the government. hey publish maps of the country showing the two ortality figures in various regions in 1946 and 1951 rom these it can be seen how the face of the land is being verspread by this dark shadow

MYXOMATOSIS AT LARGE

IN the autumn of 1952 the myxoma virus escaped om a private walled estate in the French department f Eure-et-Loir where it had been deliberately planted, nd within a year it had spread among the wild rabbits 29 departments [1] Today every department is affected, lthough to a varying extent thus, the animals round aris and Marseilles have suffered much more severely han those in the south west of the country The pidemic is now spreading through Belgium Holland nd Germany where hundreds of millions of rabbits ave already died; and last month the disease was dentified in Kent and Sussex. The incubation period f this horrible infection may be as long as ten or twelve ays before the onset of blepharitis, which is followed y the more severe lesions on the ears and head, the kin and the anogenital region Not every animal hows the typical features, and the French report that hey have seen infected rabbits with very few obvious gns. Terminal pasteurella infections are common and ay confuse investigation. In France this epidemic has aused bitter public feeling not only because of its ffect on a national sport but because there is less meat or the poor, and fewer pelts, both from wild and tame abbits, for the important fur trade

Now that the virus has crossed the Channel we must e prepared for it to spread rapidly but there are few pidemiological data [2] on which to base predictions ustralian workers have shown that several species of osquito can transmit the virus mechanically and this robably explains widely scattered outbreaks. Brereton's elief [3] in a steady creeping advance of the epidemic, t the rate of some three miles a day suggests a more ntimate method of spread. So far there have been no eports from the French biologists who are investigating he disease in the field Jacotot and his colleagues [4] at he Pasteur Institute have found that when uninfected nd infected animals are kept in the same cage trans mission does not necessarily follow On the other hand ven when infection was introduced by pricking the skin ith a contaminated needle only 3 out of 250 laboratory nimals showed a natural resistance to the virus. It lso seems that when a fresh stock of rabbits is introduced nto an area previously cleared by the virus they are nable to withstand the disease for more than a few eeks Probably both methods of spread are important nd if the virus behaves like other members of the ox group various contaminated materials will transmit he infection If this is so then it is unlikely that easures now being taken in Kent and Sussex can do ore than contain the infection for a short time

Before they released the virus the Australians showed conclusively that it attacked only the European rabbit or its more elegant tame descendants, and that it was quite incapable of infecting other closely related species. The hare in particular was thought to be naturally immune but Jacotot and his colleagues [5] have proved that at least one true hare has died of the disease There are two types of hare in France: one is really a rabbit in disguise and may be fully susceptible; and the other is the more usual brown hare The hare examined by Jacotot had the typical lesions of the disease and ticks (*Ixodes ricinus*) recovered from its skin, were capable of infecting rabbits. Attempts to transmit the disease to two other hares were unsuccessful and the conclusion is that infection among hares is probably rare. Apart from the possibility that the red squirrel may be susceptible no other species has so far been infected and the alleged human infections have not been confirmed by laboratory tests It seems that the calculated risk first taken by the Australian workers, who judged the myxoma virus to be stable has so far been justified although no one can be certain that the immunity of other species will last.

UNITS

THE expert committee on biological standards of the World Health Organisation have announced [6] the second international standard for penicillin This step has been necessary because the stocks of the first standard have been exhausted. The new international unit is defined as the activity contained in 0 0005988 mg of the second international standard for penicillin The occasion has been taken by Miles and Perry [7] to discuss what is meant by a unit of a biologically active substance, and on what principles the unit should be determined. The clinician who prescribes such drugs as insulin, heparin calciferol and corticotrophin (A C T H) in terms of units may come to think of these doses as directly representing the therapeutic efficacy of these drugs in man This is not the case: and for important reasons The unit if it is to have meaning must be as nearly as possible an accurately reproducible quantity So complex are the actions of a biologically active substance in the human body, and so many variables may modify the response that assay in man could not allow a unit of constant value to be accurately defined Assay must therefore be made in terms of a definite and measurable activity of the substance in a controlled biological system For example, corticotrophin is assayed by its ability to reduce the ascorbic-acid content of the adrenal gland of the rat after intravenous injection In man this property may not directly represent a desired therapeutic effect of the drug and the physician must learn by experience what effect he is likely to obtain from a given dose in units

This argument is not purely formal but has important practical bearings A substance may possess properties not measured by the current method of assay which nevertheless profoundly modify its action in man Thus, a new preparation of corticotrophin was shown to be of equal potency with the older preparation when assayed by intravenous injection in the rat The same substance was found however to have four times the therapeutic efficacy of the previous preparation after intramuscular injection in man The two preparations were equipotent by intravenous injection in man and the difference between them was presumably related to absorption How is the information about the different properties of the two preparations to be logically conveyed? The method of assay in the rat could be changed to use the intramuscular route But this complicates the biological system in which the assay is carried out, introducing factors difficult to control and thus endangering the reproducibility of the unit. The unit of the new product could be quadrupled, but this would create as many problems as it solved. Since the product cannot be assayed in man, it is assumed that the ratio of intramuscular to intravenous efficacy is the same for the test animal as it is for man—an assumption which at present lacks proof. Another possibility would be to introduce a second unit, but this hardly seems justified for a substance which differs so far as is known only in one property—namely, intramuscular efficacy—from the older corticotrophin. The temporary solution suggested by Miles and Perry is to describe the new product as "corticotrophin H I M"—meaning "high intramuscular activity"—and leave it to the clinician to familiarise himself with the significance of these initials.

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[1] The Lancet Aug 15 1953 p 333
[2] Ibid 1953 ii, 278
[3] Brereton, J L G *Nature Lond* 1953 172 108
[4] Jacotot, H., Vallee, A., Virat B Meeting of Académie Vétérinaire Oct. 15 1953.
[5] Jacotot, H., Vallee A, Virat, B Meeting of Société de Microbiologie, Nov 5 1953.
[6] Humphrey J H., Mussett, M V Perry W L M *Bull World Hlth Org* 1953 9 15.
[7] Miles A. A., Perry W L M *Ibid*, p 1.

Miles and Perry discuss similar difficulties arising from the proposal to establish an international unit for adsorbed diphtheria toxoid. This should be defined in terms of its content of plain toxoid, which in turn depends on the content of *Lf* units. The addition of, for example, aluminium greatly enhances the immunising power of the product in man without altering its content of toxoid. One unit of the adsorbed toxoid might then have the same immunising power, and thus the same significance to the clinician, as 100 units of the plain toxoid. Therapeutic efficacy is clearly not the same as potency; nor is it an acceptable basis for defining the unit. The unit is a statement of the amount of active principle present in a drug, as determined by an assay of its activity in a controlled biological system. This definition of the unit is essential to its fundamental property—exact reproducibility. Miles and Perry emphasise that it falls to the clinician to determine how a unit thus defined is related to therapeutic effect. He may sometimes be tempted to look upon the standardiser of biological preparations as his handmaiden, and this emphatic statement of principles may perhaps disturb him. But a servant with firm principles is often a very good one, and the views of Miles and Perry are in keeping with the best interests of all who use drugs that have to be standardised in this way.

THE HUMAN FEMALE

THE much-publicised second volume of Dr Kinsey's monumental research on human sexual behaviour is now available in this country.[1] The new book, a worthy successor to its predecessor,[2] is a serious, well conceived, and courageous attempt to provide factual information about a branch of social psychology in which legend and emotion still predominate over knowledge and sense. It should be particularly welcome to doctors even if they feel uncomfortable that it has been left to a comparative zoologist to open up this field. The inspiration belongs to the school of Lorenz and Tinbergen rather than that of Charcot or Freud. It is to the general public, however, that Dr Kinsey's work is really directed—it is the ordinary citizen who suffers most from the ignorance or fanaticism of his sexual mentors, who has to make up his mind on issues of personal morality, and who today is demanding factual information on which to base his judgments. In upholding his right to have such information, the authors of this book stand explicitly in a tradition of American liberalism which cannot fail to be reinforced by their example. The opening chapters, in which they defend that proposition against the irrational and the coercive attitudes in modern society, is a remarkably dignified contribution to that tradition.

The statistical material is based on 5940 case histories obtained by methods similar to those in the previous survey. The interpretation of data so obtained is inherently difficult, since the need to secure full cooperation from the subjects prevents conventional probability sampling, and instead the subjects were obtained by securing the cooperation of groups (detailed in the text) and interviewing, whenever possible, all the members. The recurrent press criticism that the subjects are abnormal and exhibitionistic volunteers is probably unfounded in fact, but the limitations of the sampling method require to be borne constantly in mind, and a more restricted general title for the book might have served to underline these, and the authors' awareness of them. Reference to "the human female" would not have pleased Karl Pearson, despite the authors' explicit disclaimers.

The statistical material on frequency and character of "sexual outlet" is if anything rather better presented than in the earlier study, and is a good deal easier to assimilate. A definition of sexual outlet in terms of orgasm alone may offend the Freudians, but there is much to be said for it in a study where some arbitrary form of categorisation is essential, and it is refreshing to see a work of social anthropology in which the word "sex" is permitted to retain some over all connection with specifically reproductive behaviour. The data concerning prevalence of various forms of sexual activity contain little which will be new to any working social psychologist, though they may surprise others. Perhaps the least expected findings were the high incidence (26%) of extramarital relations in married women, and of orgasm following erotic dreams (40%), a subject on which little previous work has been done. As in the previous book, Dr Kinsey presents much material which will lead to serious rethinking of our attitudes to childhood and adolescent sexuality. More important than the statistical material, from many points of view, is the careful review of the physiology of sexual stimulation and of orgasm. No other important physiological process has been so little studied. Quite disproportionate harm and unhappiness is often caused by inadequate sex relations. The expulsion of the legendary and the anecdotal can be very simply achieved by providing an occasion for comparing notes, and this is an important undertaking in itself.

The whole study, though exhaustive and occasionally exhausting, has the very high merits of humanity and a good deal of dry humour. Dr Kinsey's team has already deserved very well of public opinion, but its most important work is yet to come, in the impending study of the attitude of the Law and the penal system toward sexuality, which is promised as the next in the series. This attitude is widely regarded, and not only by "armchair reformers," as one of the least civilised and most discreditable aspects of modern Western societies. Dr Kinsey has already shown that if the laws restricting sexual conduct could be fully enforced in the United States, 95% of the male population would be in prison. The consequences of prosecuting homosexual offenders, especially when such cases follow a wave of ill informed public emotion, such as appears to be threatening here at present, are far more serious, and fall on a far greater number of victims, than the consequences of the behaviour which is being so savagely punished by society. It requires little imagination to see that a penal system can be based on the assumption that sexual activity can be indefinitely suspended in healthy adults is at variance with reality. The study of sexual behaviour makes it increasingly difficult to shelve or ignore such problems as these. We are becoming aware that many traditional attitudes are often painfully akin, themselves, to psychopathology, and that the inspiration behind much sexual legislation does not come from the best adjusted or most reasonable section of the community. "Somehow," writes Kinsey in his preface, "in an age which calls itself scientific and Christian, we should be able to discover more intelligent ways of protecting social interests without doing such irreparable damage to so many individuals nd to the total social organisation to which they belong the work of the Indiana University team has no other sult it will have achieved a major philanthropic purpose emphasising this fact alone

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[1] Kinsey, A. C., Pomeroy, W. B., Martin, C. E., Gebhard, P. H. Sexual Behavior in the Human Female. W. B. Saunders. Philadelphia and London. 1953. Pp. 842. 50s.

[2] Kinsey, A. C., Pomeroy, W. B., Martin, C. E. Sexual Behaviour in the Human Male. Philadelphia and London, 1948.

NIGHT SHIFTS

INCREASED production is continually being demanded British industry and the question of night shifts, make the best use of personnel and of factory space nd equipment, demands the closest attention Wyatt nd Marriott,[1] of the Medical Research Council group for search in industrial psychology throw some light n the factors affecting the morale and efficiency of orkers on night shifts and on the relative effects of eekly fortnightly and monthly alternations between ay and night shift work.

Data collected in 1946–49 in three factories (A making ilway wagon wheels B a rolling mill and C making otor vehicles) all employing men and having respec vely weekly fortnightly and monthly changes from ay to night shift were closely studied and a number of en from each factory were interviewed to ascertain heir attitudes. Output records from two of these ctories together with those from eight others—making total of three on weekly shift-changes four on fortightly changes and three on monthly changes—howed that the average hourly output was slightly ss on night work Wyatt and Marriott point out owever that the night worker being paid at a higher ate may reduce his output in order to keep to his esired wage level without undue exertion Of 150 en questioned about their opinions of their efficiency n day and night work 68% claimed to work better by ay 21% reported no difference and 11% thought they orked better by night The attitude of the individual as related to the effects of shift changes upon his sleep nd eating habits.

In the four factories with fortnightly alternations f shifts, comparison of the average hourly output in he first and second week of day shifts showed that it as slightly higher in the second week—which suggests hat the effect of two weeks on night shifts carries ver to the beginning of the following day-shift period. In ten factories engaged on various types of engineering nd using the fortnightly alternation of shifts the bsentee rate was higher on the day-shift period (8 89% f possible shifts, as compared with 7 00%) These igures however included permanent day workers who might be unfit for night work Other complicating factors are the greater counter attractions outside the factory for the day worker and the high rate of absence on Saturday mornings. Accident-rates of 13 962 men in five factories were slightly higher for night work, but the difference was not statistically significant.

Wyatt and Marriott remark that opinions expressed by the workers are likely to reveal important and unsuspected aspects of the situation that are not disclosed by objective records. A sample of 150 men from factories A B and C were carefully interviewed. Almost all the men preferred the day shift—41% because it gave them the evenings free About a third said they felt better on day shift especially as regards sleep 20% said they had a better appetite and digested their food more easily; 34% disliked night shifts because they could not get enough sleep by day When asked whether they would opt for a weekly fortnightly or monthly alternation of day and night shifts a majority in each factory opted for the existing system—an example of the general tendency of workers to prefer what they are accustomed to Questioned about fatigue 83 3% said that they felt more tired on night shift and only 8 7% on days the remaining 8% noticed no difference Almost all the men brought sandwiches to work; 70% preferred to bring their own meals rather than eat the canteen food 74% said they enjoyed their food better when on day shift. 65 of the 150 took patent medicines regularly mostly for stomach disorders, and 33% also took aspirin fairly often 24 men had occasional indigestion and 7 more had continuous indigestion Wyatt and Marriott suggest that quite apart from the irregular meal times, the diet of most of the men was unbalanced; it seemed that they received no guidance on the subject either in the factory or outside In the matter of sleep 83% adapted themselves immediately on changing from night to day shift but only 50% in the reverse direction. 42% said they could not get enough sleep by day 37% had less than six hours sleep by day while 75% had less than eight hours

Wyatt and Marriott conclude that far more attention should be given to the selection of workers for night shift and to the medical supervision of those selected They suggest that the fortnightly alternation of day and night work is probably the best.

TESTS OF SPERMICIDAL ACTIVITY

CONTRACEPTIVE pastes and jellies designed to be used with or without a rubber appliance, should combine rapid spermicidal action with a mechanical barrier effect But by giving a compound greater viscosity one may prevent the escape of the active spermicide into the semen Thus in studying the efficacy of a contraceptive product we need to measure not only its total spermicidal power but also the speed and completeness with which the spermicide will get out of the base and attack the spermatozoa. For this purpose J R Baker devised the diffusion test but it has technical disadvantages Davidson[1] has therefore proposed a modification, which he calls the contact test, in which spermicide and semen are brought into contact on a special slide, without mixing or mechanical disturbance Another test with the same object, had previously been described by Gamble.[2]

In Davidson s test a layer of semen 1 mm thick lies on a similar layer of contraceptive in a sealed cell 5 mm. in diameter through the roof of which the spermatozoa can be observed Gamble s test is carried out in a piece of glass tubing 20 mm. long with a lumen 2 mm in diameter The tube contains a column of air 5 mm long a column of semen 5 mm. long and a column of the paste or jelly to be tested 10 mm long The ends are sealed with wax and the tube laid horizontally on a glass slide The surfaces of the jelly and semen are in close contact.

The principle of the two tests is the same and both have the merit of using very little semen (Davidson 18 8 c mm Gamble 15 7 c mm) which allows several tests to be made with one ejaculate The difference lies in the area of contact between the semen and the contraceptive. In Davidson's test this is 18 8 sq mm while in Gamble s it is a little more than 3 sq mm It is generally accepted that there is almost no movement of molecules through the matrix of the jelly and that only the surface layer will yield spermicide to the semen so the maximum concentration of spermicide from a given contraceptive should be more than five times greater in Davidson s test than in Gamble s. Moreover in Davidson s slide none of the spermatozoa are more than 1 mm from the surface of contact whereas in Gamble's tube the spermicide must be distributed through the 5 mm column of semen before all the sperm are affected by it Gamble attributes the streaming in the semen which ultimately leads to the death of all the spermatozoa, to convection currents set up by changes in density of the semen as it dissolves the spermicide, in which case the rate of mixing would be proportional to the rate of solution but streaming may also be produced by changes of temperature, and their effect on the air in the tube. With Davidson's test, satisfactory substances kill all spermatozoa in half an hour. Gamble's test naturally takes much longer but this carries some advantages. The viability of human semen deteriorates quickly, and the resistance of spermatozoa to toxic chemicals, especially at body-temperature, falls with delay; so the value of tests taking over three hours is rather questionable. Within this time, however, the rate of immobilisation of the spermatozoa is more gradual; and it is possible to compare the rates at which contraceptives act, and (provided the results for each substance are consistent) to arrange them in order of relative efficiency. Unfortunately Gamble's figures indicate great variation in tests with a single product: in a series of tests with a standard deviation of 38% of the mean, and an average of two hours for complete immobilisation of the spermatozoa, the individual results could range from half an hour to three and a half hours. This degree of variance is so great that it is difficult to suppose the grading of contraceptives would be more accurate than with Davidson's method. The principal merit of Gamble's method, as we see it, is that, instead of a special slide, glass tubing—which is always available—can be used; though this has the drawback that spermatozoa are hard to see through the side of a cylindrical container.

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[1] Wyatt, S., Marriott R. *Brit J industr Med* 1953 10 164

[1] Davidson H A. *Lancet*, Aug 29 1953 p 439

[2] Gamble C J *J Amer med. Ass.* July 11 1953 p. 1037

Neither test, of course, is intended to reproduce conditions in the vagina; but it is hard to see why Davidson vetoes the use of incompletely liquefied or persistently mucoid semen. Such semen, being exceptionally resistant to the passage of spermicides, would certainly increase the time taken in the test; but contraceptives always have to act on freshly ejaculated semen, and often on mucoid specimens, and it seems reasonable to suggest that every commercial preparation should be tested at least twice against such ejaculates.

ADOPTION AND MENTAL HEALTH

To be deprived of a natural mother and taken over by a substitute, however loving, inevitably exposes a child to emotional risk. The joint United Nations and World Health Organisation meeting of experts on the mental health aspects of adoption, who have just reported,[1] have concentrated on seeing how far this risk may be minimised. To advise the whole world on such a subject is not easy, because customs differ so greatly from East to West: they have therefore concerned themselves chiefly with the principles on which adoption procedures are based in Western society.

They restate at the outset the now well accepted belief that adoption is the most complete means of restoring family life and relationships to the child without a family. The satisfaction of the desire of childless people for children is, they think, of secondary importance. Most children in need of adoption are illegitimate, which means, as a rule, that they can be adopted in infancy. Sometimes, however, a mother who wants to keep her child manages to do so until he is two or three years old, and then finds that the difficulties are too much for her. Separation can then be a bitter experience for both mother and child. The report also mentions the particular situation of brothers and sisters deprived of both parents: they naturally cling together, and it is very doubtful whether it is wise to allow them to be adopted singly, unless groups of adopting parents known to each other will each take one or two of them. This is not easy to arrange, and of course brings its own stresses; but it is perhaps better for the family than an institutional upbringing would be.

Any child who is adopted needs to be able to count on the continuance of loving care. The parents must be able to offer him a whole-hearted acceptance, taking him as he is, giving him not only love but a chance to love back, and letting him blow off, without too much guilt and anxiety, the conflicting and often hostile feelings to which frustrating reality makes us all a prey. In fact he needs normal mothering and a home where he can make normal relationships with a father, other children, relatives, and friends. If he is more than a few months old he should have some chance to get to know his new family before he goes to them, and if he is old enough to notice toys he should take a favourite one with him to his new home. The expert group, however, were dubious of the practice followed by some adoption societies of placing the child with its adopting parents for a trial period—usually three months—before adoption is decided on. This is said to give the real mother time to reconsider the position, and change her mind if she wishes, and also to allow the adopting parents to find out whether they like this particular baby; but it is an arrangement which carries considerable emotional risks for all parties—for the mother because it exposes her to disqueting doubts and fosters her almost inevitable sense of guilt about the transaction, for the adopting parents because they may either become too fond of a baby whom they suddenly abruptly lose, or because they feel their motives are being scrutinised suspiciously, or because warm acceptance of the child as he is may be replaced by a mood of appraisal, and for the child, above all, because it exposes him to a chance of being bandied about from one mother to another. If we accept the needs of the child as paramount it must be agreed that, for him, the trial period has serious drawbacks which are hardly outweighed by the gains.

The group think it important to make sure of the motives of the would be adopters, and their attitude to the child. If they want him because a child of their own has died they first need time to resolve their sense of grief and loss; if they are hoping he will patch up an unhappy marriage, or if he is expected to resolve the neurotic problems of one of the partners, they are putting their own needs first. Single women (except the child's mother) and widows are liable to have mixed, partly selfish, motives, and it is therefore thought better for the child to be adopted by a married couple. The natural mother ought to be given practical information and advice by a trained and well balanced person, so that she can decide freely whether to keep her child or have him adopted; and of course the adopted child should be given legal status which entitles him to the same opportunities and rights as a child in an ordinary family. Adopting parents should not have the right to repudiate the child later if he turns out badly. The group believe that the child should know from an early age that he has been adopted.

Some interesting though tentative suggestions are made about the adoption of handicapped children. There are some people whose warm parental feeling fits them to look after a child with a handicap; and it has been found that adoptions of this kind can turn out well, provided the child's needs and the suitability of the home are carefully studied.

THE Nobel prize for physics has been awarded to Prof FRITS ZERNIKE of the University of Groningen "for his phase-contrast methods, particularly the invention of the phase-contrast microscope."

IN the New Year the editorship of *Brain* is to pass to Sir RUSSELL BRAIN, F.R.C.P., on the retirement from this appointment of Dr F M R WALSHE, F.R.S.

Dr CHARLES F MARTIN, dean of the faculty of medicine of McGill University from 1923 to 1936, and president of the American College of Physicians in 192-29, died in Montreal on Oct 28, at the age of 85.

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[1] *Tech. Rep Wld Hlth Org* no 70. H.M. Stationery Office 1953 1s 3d

Reconstruction

CENTRALISATION IN THE HOSPITAL SERVICE*

The Need for a Change of Policy

THE National Health Service Act of 1946 opens with he words

> 'It shall be the duty of the Minister of Health (hereinafter in this Act referred to as the Minister) to promote the establishment in England and Wales of a comprehensive health service designed to secure improvement in the physical and mental health of the people of England and Wales and the prevention diagnosis and treatment of illness and for that purpose to provide or secure the effective provision of services in accordance with the following provisions of the Act

This introduction illustrates not only the extremely wide rope of the health service but also the extremely wide ange of the duties of the Minister himself At the same ime these duties are defined only in very general terms n the Act as are those of the Minister s agents the oards of governors regional hospital boards, and hospital nanagement committees

In outline there is a three-tier system of administration nvisaged for non teaching hospitals

The Minister—Regional Hospital Boards—Hospital Management Committees

ogether with a simple two tiered system for the teaching hospitals :

The Minister—Boards of Governors

The Minister is responsible only to Parliament He is o administer through his agents, the boards who dminister through their agents the management com nittees, Existing side by side with this agency method f administration is the direct legal responsibility of a rincipal which is granted to regional hospital boards, oards of governors, and hospital management com nittees (notwithstanding that they are exercising unctions on behalf of the Minister) While the Minister hay therefore impose his will upon each or any of his gents by regulation or direction these agents have a lirect legal responsibility for their actions

Nevertheless this administrative framework though t embodies the agency principle is so constituted as to llow at the Minister s discretion centralised direction n all matters both large and small by liberal use of the dinister s reserved powers subject only to the require nent that the Minister must lay statutory instruments efore Parliament within a prescribed period It is equally onstituted to allow the administration to be entirely lecentralised, and for virtually all responsibility to be laced in the hands of boards and management com nittees acting as agents for the Minister

Intentions

It could be argued that the Act in itself was conceived n a spirit of mistrust While powers are given, all may e negatived if they are not used as the Minister wishes. nstead of being obliged to make the delegation of uthority and responsibility a real working arrangement he Minister can always fall back upon the escape clause f reserved power However in order to allay this feeling f mistrust, the Minister at the time (Mr Aneurin Bevan) nd his Parliamentary Secretary (Mr C. W Key) were t great pains to explain their intentions

> ' This scheme provides that the Regional Boards with their local Management Committees are to enjoy a high degree of independence and autonomy within their own fields —Mr KEY (*Hansard* vol. **422** no 129 col 208)
>
> Moreover, the Boards, and under them the Hospital Management Committees will have a very considerable amount of financial freedom as far as administration is concerned. At the beginning of each financial year they will prepare their annual estimates. Their budget, of course, will have to secure approval but when once it has been approved it will be for the Board to spend the money, put at their disposal by the Exchequer, as they think best, up to the limit of the sum that has been approved. There will be a wide discretion concerning that global sum, and not, as some critics tell us, central control over the detailed items of financial expenditure. —Mr KEY (*Ibid*, col 209)
>
> The central principle of the Bill under which the House places on the Minister the responsibility for these services inevitably means that he must have agents. Every single instrument must be an agent, because when any instrument ceases to be an agent the contract is broken Having established that principle it is then necessary to provide that the central responsibility which the House *places upon the Minister to provide a service does not result* in that service becoming too highly centralised in its administration That is precisely what the scheme provides. It provides for the establishment of Regional Boards ; it provides for Management Committees and for House Committees. In fact the scheme, right through, provides for measures of decentralisation so that individuals in a locality can have as much influence as possible over the medical and hospital services —Mr BEVAN (*Hansard* vol **426** no 185 col 469)

In this way the Government defended their proposals, arguing that only by giving the Minister these wide discretionary powers could there be provided the flexibility of administration necessary for the development of the new health service, and at the same time emphasised again and again their intention that the *administration of the service should be decentralised* as much as possible

The Government's good intentions were repeated in the early circulars that were issued to hospital authorities from the Ministry

> " Broadly, the effect of this administrative structure is that the function of the Regional Board is to determine in consultation with the Minister and as a fluid and constantly developing process the part which each hospital is to play in the integrated service to deal with wider regional problems, and to oversee the operation of the hospital service of their area ; that of the Management Committee is to administer its hospital or group so that it plays its part in the most effective manner Powers of central control are reserved to the Minister because of his ultimate responsibility to Parliament " (R.M.C 48/1)
>
> In framing the Regulations the Minister s object has been to avoid proscription in detail of the manner in which the various bodies are to perform their functions, and by laying down division of responsibility in broad terms to allow the greatest measure of flexibility and variety in administration. His desire is to rely on ordinary methods of guidance by way of advice on questions of policy and not on a detailed code of rules embodied in regulations, for the purpose of maintaining the necessary degree of unity and homogeneity *in the service It is however essential that there should* be reserved to him (as is reserved by the Act) an ultimate power of laying down the manner in which the various functions are to be performed. The Minister s intention is that these ultimate powers should be exercised as infrequently as possible and that normally the ordinary processes of administration will suffice to ensure that the general policy of the service is observed (R C 48/)

Perhaps the clearest statement of policy of all was that contained in the memorandum submitted by the Ministry to the Select Committee on Estimates in 1950

> It has from the outset been the policy of the Minister to allow a wide *measure of independence in hospital* administration to the hospital authorities subject to necessary

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* Based on a memorandum prepared for the Hospital Discussion Group by a small working party of hospital administrators. The members of the working party were A. H. BURFOOT B.A A.H.A., M C HARDIE M.A R P K MACMAHON M.A. J W MARSHALL, M.A., and J L. C SCARLETT M.A

financial control from the centre The main instruments of that control are

(a) Submission by each hospital authority of an annual estimate, with a revised estimate in the autumn
(b) Formulation of policy in its major features by the Department, which is communicated to the hospital authorities in circulars and memoranda,
(c) Regular periodical conferences with officers of the Ministry of the Chairmen of the Regional Hospital Boards and of the principal officers of Boards,
(d) National determination of salary and wage scales and conditions of employment, &c ,
(e) Monthly returns from the hospital authorities of their expenditure and income,
(f) Liaison through Regional Officers of the Ministry, who may attend the meetings of the hospital authorities and who receive their circulated papers,
(g) Central purchase by the Department of certain supplies,
(h) Current audit of the accounts of the hospital authorities by officers of the Ministry,
(i) Development of a system of hospital costing "

Had the Ministry adhered more closely to this policy it might well have avoided the present widespread criticism of over-centralisation in the hospital services But neither intention nor policy has been entirely fulfilled

Finance

Centralisation of some kind is as inevitable as it is desirable, and the extent of it envisaged in the early circulars cannot fairly be considered either excessive or oppressive

In subsequent years the financial circulars have generally continued to be basically reasonable, and the Minister's financial policy has usually been as flexible as could be expected under the circumstances, and within the framework dictated by the Parliamentary necessity for an annual vote of funds It is in fact the external circumstances that have been responsible for much of the centralisation that now exists funds for hospital building work have been controlled not so much by the needs of the hospital service as by the necessities of the national capital investment programme, policy on salaries and wages (which account for over 60% of hospital expenditure) has been affected by Cabinet decisions, as at the time of the devaluation crisis in 1949 and of the Chancellor of the Exchequer's statement on the stabilisation of personal incomes, and, since there is practically no theoretical limit to the amount of money that could be spent on the Health Service, the annual allocation of Exchequer funds has been determined by the national economic situation, which has called for great financial stringency.

All these factors have combined to increase the centralisation of financial control, and in addition it must be remembered that in the first two years of the service the cost of the hospital service was grossly underestimated, that there has as yet been no accurate method of assessing hospital costs and comparing the relative efficiency of different hospitals, and that all hospital authorities, from the Ministry downwards, are still in process of learning the facts—and particularly the financial facts—of a national hospital service

It is not surprising, then, that there has been greater centralisation than was originally intended But such centralisation may not always achieve either the greater efficiency or the greater economy which are its objectives While the attainment of these objectives must depend largely on improved hospital accounting and costing, two points are worthy of consideration now

(1) The need to give hospital authorities some incentive to effect economies and savings Real savings can be effected only at the hospital level, and it is there that the incentive is needed possibly by allowing savings on the annual budget to be used for the development of hospital plans or for the purchase of improved equipment, at an earlier date than would otherwise be the case

(2) The development of a modified system of block grants for building maintenance and capital expenditure, and a redefinition of these terms Such expenditure would be much more efficiently planned and carried out on a five year basis

In the financial field, therefore, it appears that the form of centralised control is generally reasonable in the light of all the circumstances It is centralised control in other than financial and related matters that causes much of the present discontent

The problem can be considered at two leve[illegible] isation at the Ministry and centralisation at the regi hospital boards

Centralisation at the Ministry

Much of the evidence on this can be taken from the Ministry of Health memoranda issued since 1948 T circulars go to regional hospital boards, hospital management committees, and boards of governors—so to only one or two of these authorities but generally all three simultaneously Until the end of 1952 the t number of circulars issued was

To regional boards	64
To hospital management committees	537
To boards of governors	38

This works out at approximately one circular every [illegible] days to every single hospital authority in the country

Almost every one of these circulars could be justif as being reasonable in its substance and many are in fact concerned with Whitley Council decisions of [illegible] all hospital authorities must obviously be informed Nevertheless, in spite of their general reasonableness and of the ease of filing and reference to them, the system cannot be regarded as satisfactory The recipient [illegible] smothered by the quantity of circulars, some of which not apply to his particular hospital or group, and are issued in the same form, whether mandatory advisory, important or unimportant The general e[illegible] of this is to decrease the attention paid to circulars the hospital authorities, and at the same time to en a dangerous feeling that everything will be covered a circular sometime or other, and this feeling inevitably diminish the sense of individual initiative responsibility that is an essential prerequisite successful management Furthermore, since these [illegible] lars are generally issued by the Ministry simultane to regional boards and management committees, responsibility of the regional boards becomes correspondingly diminished, and it may be difficult for t to fulfil in a true sense their acknowledged rôle of a[illegible] for the Minister and principal for the management committees

More positive advantages might well result from alternative method of distribution, which would [illegible] properly recognise the agency principle In outline the alternative would involve

1 Mandatory circulars to be issued to all hospital authori only when conveying decisions which affect all and on w no local discretion is permissible, such as decisions on of pay or conditions of employment agreed by the Whitley Councils, decisions on charges for appliances, pay t prescriptions, &c , and decisions arising from national pol on such matters as capital investment or Civil Defence

2 All other circulars conveying general guidance advice to be issued only to regional boards (or to boards governors where appropriate), who should be trusted to their own judgment and discretion on the best method implementing them in their respective regions, in co[illegible] with the hospital management committee concerned

This method would give the regional boards [illegible] responsibility, and would also allow greater scope intelligent discrimination in "putting over" the Minis ter's policies Most important of all, it would mark return to the original idea of the principal agent relationship between the Minister and the hospital authori pon which the whole administrative structure of the ospital service ultimately rests

The structure itself has often been held to blame for e faults of the hospital service but this criticism can ardly be considered valid, because the principles on hich the service was based have not been properly bserved It would therefore be premature to condemn e structure at this early stage of the health service d to advocate its replacement as some critics have one, by a revised local authority type of administration, by the creation of a National Hospital Board ith powers and responsibilities similar to those of the ational Coal Board Such extreme measures cannot justified until the present system has been given a ore thorough trial and the most important thing to at the moment is to put into practice the principles hind the present system

HE CIVIL SERVANT AND THE HOSPITAL ADMINISTRATOR

Administratively, the success or failure of the hospital rvice depends very largely upon the establishment of e highest possible degree of mutual confidence and spect between principal and agent at every level and this vital matter there is a great need for improvement

The first point that needs to be emphasised is the fference between the rôle and methods of the Civil ervant and those of the hospital administrator whether edical or lay The rôle of the Civil Servant in relation the Minister is comparable to that of the administrator his board or committee in that each is an adviser d an executive but in addition the hospital adminis rator is responsible for the day to day management of e hospitals under the control of his board or committee his means that in reaching any decision the adminis rator must give great weight to the human factors volved, taking into account his confidence in the staff ncerned and his assessment of their abilities and his ethods will naturally differ from those of the Civil ervant, who is concerned with the comparatively personal problems of the planning and development a nation wide health service rather than with the mediate practical problems of management

In view of this difference of function between Ministry d hospital authorities a difference of administrative ethods is both natural and desirable and given a reason ble measure of respect and understanding on either side hould not lead to difficulty or antagonism What ppears to cause both difficulty and antagonism at the resent time is the tendency of the Civil Servant to apply every level of the hospital service the methods of personal administration that are suitable for the entral functions of the Ministry but not for the day -day management of individual hospitals or hospital roups

Another possible source of misunderstanding is the ct that in the event of any administrative mishap or stake the Minister accepts public responsibility for e failings of his officers at the Ministry who rightly reserve their anonymity whereas if a board or com ittee is criticised not only is its good name publicly stake but also that of the administrator It is not ggested that this position should be altered but it is portant to recognise that there is this difference in ublic accountability

The situation is made more difficult by the fact that he Ministry has assumed responsibilities which it was ot originally intended that it should, and for which ivil Service methods are not properly suited. The need r extreme financial economy has—understandably but one the less regrettably—led the Minister to impose a ntrol over administrative detail, and this control has roused considerable antagonism

Though the financial situation is largely responsible, art of the explanation can be traced back to the theory put forward by Mr Bevan in the debate on the National Health Service Bill during the Committee stage (col 208) when he said

> I must ask hon. Members to assume that the wide body of knowledge at the disposal of the Ministry of Health, with the very many technical advisers available both voluntary and otherwise is much more likely to produce a good hospital design than a local management committee.

Although in this case the theory was applied only to hospital design, it has in fact been applied to many other aspects of the hospital service—and indeed of the whole national economy—and it can be briefly summarised in the now famous remark that ' The gentleman in Whitehall really does know best

Logically there is something to be said for the idea that the Ministry of Health should be the centre of knowledge able to draw upon the experience and wisdom of technical advisers and experts, who in turn, by virtue of their position at the heart of the nation wide organisation of all the health services are theoretically in a position to see all sides of every question and to provide all the best answers. In practice however this theory is open to several criticisms Firstly there is a danger that the advice of experts appointed and controlled by the Ministry will be heard and accepted to a greater degree than that of the voluntary part time advisers, who are generally chosen from practising members of the professions and organisations concerned with hospitals Secondly the Ministry experts are not necessarily the most competent persons in their field and are therefore not necessarily the persons to set the standards for the whole hospital service Thirdly the experts by reason of their work at the centre tend eventually if not rapidly to become out of touch with the day to-day realities of hospital work Fourthly when this theory is applied to the details of hospital work—as it has been applied by the Ministry—it means that the experts bring upon themselves an enormous load of work, which inevitably leads either to inordinate delays or to insufficiently considered decisions and which also throws a great strain upon the Ministry officials concerned, not only because of the pressure of work but also because the methods of the Civil Servant are hardly suited to this type of administrative work Fifthly, the application of this theory introduces a large element of standardisation and uniformity in the service though desirable to a limited extent on grounds of economy these attributes of centralisation can only too easily produce unwanted rigidity and inflexibility in an essentially humanitarian service which must always be changing and developing if it is to provide the best care for the patient. Finally—and this is an argument that applies not only to the National Health Service, but also to all forms of central authority —the continued application of this theory of centralisation has an insidious effect upon the spirit of local and individual initiative and responsibility The process is made all the more insidious and dangerous by the almost imperceptible way in which it grows and of the evident reasonableness which which it is invested. As has been said earlier a study of all the circulars that have been issued shows that individually nearly every one appears to be basically reasonable and apposite The objection to the detailed guidance given in these circulars lies not in their substance but rather in the fact that it is the central authority which is in this way usurping the proper functions of the regional and local authorities and their officers. The ultimate effect of this process is inevitably a lowering of the standards and qualities of those who will be attracted to serve either as members or as officers of the boards and committees this in turn will lead to a greater degree of centralisation under the direct control of the Minister and so the vicious circle will go on with increasingly unfortunate results for the patient

Few will deny that "The formulation of policy in its major features" is the proper function of the Ministry, but is it essential for the Ministry (as opposed to a regional board or management committee) to issue detailed guidance on such matters as supply of razor blades to patients, issue of sweets to children, provision of telephones for hospital staff, washing down of walls and paintwork, and detailed control of establishments? Complete standardisation on such matters, and on many others, makes for administrative convenience and tidiness at the expense of individual judgment, initiative, and responsibility Detailed control and advice on these aspects of hospital life could safely and more satisfactorily be left to the individual authorities or their officers This does not mean that the reports of the various statutory advisory bodies should not be circulated to all hospital authorities, but there is no need for these to be accompanied by explanatory memoranda from the Ministry

It is nevertheless clear that powers of central control must be reserved to the Ministry, since the Minister is responsible to Parliament, and hence by necessity must deal with

(1) The "formulation of policy in its major features" and the planning and coördination of policies affecting all branches of the health service

(2) The over-all allocation of the share of the national resources of money, materials and labour to the health service including the major decisions on capital development

(3) The determination of a national salaries and wages structure for the health service

(4) Negotiation, consultation, and direction on matters which are obviously national in application, such as Civil Defence arrangements, health service charges, and proportion of pay-bed accommodation

The acceptance of this pattern of Ministerial responsibility would of itself provide the answer to the question of the responsibility of the regional hospital boards, as put by the Select Committee

> "The Ministry either must decide to give greater scope to the Regional Hospital Boards than they at present enjoy, or alternatively they must move towards re organising the service on the basis that the functions of the Regional Hospital Boards are purely of a planning and advisory nature"

For a definition of the Ministry's responsibilities on these lines would increase considerably the scope of the regional boards There would be a twofold effect upon the administration of the hospital service In the first place the Ministry's officers would be freed from the work of detailed administrative control that they at present exercise, and would be able to concentrate not only on the actual formation of higher policy but also on the duty of seeing that that policy is in fact carried out In the second place, the increased scope and freedom from interference in detail would require of the boards an added sense of responsibility, and the relationship between Ministry and boards would have to be one of trust and confidence rather than of detailed control

The Regional Hospital Boards

Although it seems desirable in almost every way, this delegation of authority from the Ministry to regional boards could lead to the danger that there will be an excess of centralisation at the level of the regional boards

The "regional" approach to hospital development has long been considered the best method by those who have studied the question seriously, as can be seen by reference to the reports produced before 1946 by such authorities as the King Edward's Hospital Fund, Nuffield Provincial Hospitals Trust, and the Ministry of Health In each of these the need for an authority to plan and organise on a wider basis that that open to a local hospital authority has been recognised Nevertheless, the regional boards themselves have been criticised It has indeed been suggested that they should be abolished altogether, but an answer to this suggestion is that put forward by the Association of Hospital Management Committees

> "If the Regional Boards were not there the place would inevitably have to be filled by something else, which would presumably be the regional officers of the Ministry Regional Hospital Boards are essential for the planning of the hospital services, with consequential control of all major capital expenditure, *and for the allocation of senior* Medical Staff, and the distribution of available financial resources, so as to ensure the best comprehensive Health Service throughout the Region Regional Hospital Boards must also have some measure of effective control of Hospital Management Committees who act as their agents There is also the further important point that the Regional Hospital Boards are a safeguard against remote Government control, consisting as they do, like Hospital Management Committees, of voluntary workers with local knowledge"

The need for some measure of regional control is this as necessary as is the need for some central control, and the arguments against excessive centralisation are much the same in either case Now that five years have passed sufficient experience should have been gained to allow a better definition to be made, with the main object of preventing *any increase in centralisation* The regional board's functions should be to deal with those matters which from a practical point of view are best dealt with regionally in the interests of all concerned These functions, already referred to in the quotation above, can be summarised as follows

1 To plan the *hospital and specialist* services in their regions

2 To appoint the members of hospital management committees

3 To appoint senior medical and dental staff

4 To distribute the available financial resources to the hospitals

5 To control major capital expenditure

6 To maintain liaison with other health and hospital authorities—e g, county councils or boards of governors—where common policies require to be agreed *on a regional* basis

7 To act as an administrative centre for matters which are appropriate—e g, tuberculosis service, blood transfusion depots, contractual beds, and Civil Defence

8 To provide certain services for hospital management committees—e g, legal, engineering or architectural advice if required—and to help and advise hospital management committees when appropriate as part of their function of general supervision of the hospital services in the region

In other respects it should be the policy to give to the management committees as much freedom as possible, and to avoid interference in the details of day-to-day administration at present the boards are forced to interfere by the Ministry on occasions, as shown by the circular on Economy in Manpower (R H B (51) 13) Another possible limitation of the freedom of management committees lies in the fact that legally all their officers are employees of the regional hospital board The local management of hospitals, within the financial limits of the funds provided, is the function of the hospital management committees, who should be regarded as the trusted and responsible agents of the boards in carrying out these functions, just as the boards should be regarded as the trusted agents of the Minister This devolution of authority to the members and officers of boards and committees would give them a much *greater sense of* responsibility and usefulness, which would in turn ensure that really able people would still be attracted to serve in the hospital world

Although much of the criticism in this paper has been directed towards the Ministry, it would not be fair to blame all the failings upon the Minister and his officials for the boards and committees themselves are partly to blame Firstly, because, although in theory they are ponsible to the Minister (in the case of boards) or to Boards (in the case of management committees) ne authorities seem to have adopted an excessively ochial attitude which has led them to extract as ch money as they can from the Ministry and spend surplus rather than return it—a most unsatisfactory cedure, which is encouraged by the budgeting methods pted by the Ministry Secondly, because there has n exploitation of the political and emotional aspects he hospital service by some authorities in their dealings h the Ministry Thirdly because it is generally recog ed that the standard of hospital administration has been uniformly high throughout the country urthly because of the attitude of the boards and nmittees to the officials of the Ministry Many hospital horities felt deeply the loss of individual freedom essitated by the National Health Service Act and ered the service with considerable feelings of prejudice d resentment, which have found expression in resistance the Ministry s policy and regulations and in reluctance coöperate with the Minister s officials.

The relationships of the Ministry s auditors with the boards d committees provide an illustration of the general diffi ties that beset all the relationships between the Civil rvant and the hospital authorities. An independent audit a board s accounts is as essential as it is for any public com ny or corporation the fact that the Ministry s auditors o have a right to inquire into methods and practices that ly indirectly affect finance can obviously lead to mis derstandings and resentment unless tact is exercised on th sides, but this activity of the auditors is clearly necessary en one bears in mind that there are few aspects of hospital rk that do not involve finance and also that the auditors emselves cannot enforce any change of procedure but n only report From the auditor s point of view hospitals uld have been more coöperative from the hospitals point view it could be wished that the auditors would be more actical and less theoretical in their approach to any problem d it may be that with more experience they will develop wider view which at present is sometimes lacking The me comment could apply to all relationships between inistry and hospitals.

It is thus evident that there is room for improvement relationships and methods on both sides The lead can me only from the top and if the Minister shows real nfidence and trust in his agents, the hospital boards d committees will show that they are worthy of that ust. Failure on the part of the few would be best dealt ith by prompt and specific action rather than by dated and generalised guidance

Summary

1 There is nothing basically unworkable about the ructure of the hospital service as loosely defined in e National Health Service Act, nor is there any justifi tion as yet for any fundamental alteration to the Act

2. Generally speaking the underlying principles and tentions, as expressed by the Minister in the debates on e Bill, are unexceptionable and sound, although there a potential danger in the wide discretionary powers served to the Minister

3 A policy of administrative decentralisation subject over-all financial control is well suited to a national ospital service, and the statement of policy by the inistry to the Select Committee on Estimates in 1950 rovides a reasonable basis for the administration of the ospital service.

4 Although many aspects of the present financial ystem can be defended the introduction of a system ving hospital authorities some real incentive to effect vings the development of a modified system of block rants for building maintenance and capital expenditure he redefinition of these latter terms and the develop ment of hospital costing and accounting methods provide ssible opportunities for improvement

5 Centralisation has increased unreasonably in non financial matters, and there is now a definite tendency for the Minister to introduce detailed administrative control by circular thus undermining the agency principle of administration originally promised Ministry circulars should be restricted to matters which allow of no local discretion, others matters should be referred to boards for action when and where *appropriate*

6 The necessary difference between the methods and responsibilities of Civil Servant and hospital administrator can lead to misunderstandings and consequent loss of mutual confidence and respect. The Ministry should not add to these potential difficulties by introducing the detailed administrative control for which Civil Service methods are unsuitable

7 A reassessment of the rôle and functions of the Ministry is required in order to halt the tendency to over-centralisation and government by experts.' In such a reassessment the emphasis should be on the maximum possible decentralisation

8 A similar reassessment of the responsibilities of regional boards and management committees should be made with a similar emphasis upon the need to push responsibility out and down to the individual hospital authorities and their officers

9 Last and most important of all is the development of better understanding and working relationships between the Ministry and the hospital authorities. The Minister should lead the way and set the example in this change

Special Articles

ARTIFICIAL HIBERNATION

STUDIES IN FRANCE

A GREAT deal of clinical and experimental work on artificial hibernation " is being carried out in France a bibliography compiled as recently as August contained 165 references The subject was well reviewed at a recent congress in Geneva[1]

This method originated in the work of Laborit a naval surgeon who was attempting to find out whether anæsthesia could be enhanced by the use of drugs The hypnotic and sedative side-effects of Phenergan were well known and appeared to reinforce ordinary anæsthesia Laborit and his co workers carried out many experimental and clinical trials and developed techniques of improved anæsthesia with correspondingly improved surgical results At the same time 'Largactil (R.P 4560) a phenothiazine derivative, was produced by one of the large Continental drug houses This is not only a narcotic and a weak anti histamine but causes a pronounced fall in body temperature and metabolic rate It is to these two latter effects that Laborit attributes artificial hibernation *With the advent of largactil,* Laborit and his associates[2] showed, in exsanguinated dogs, that shock could be averted by hibernation induced by largactil

Clinical application quickly followed In the first instance this agent was used only in desperately ill patients; the rationale was that in severe illnesses a state of shock exists which is combated by hibernation The results were apparently good; and its use was then extended to prevent shock by reinforcing anæsthesia for major surgical procedures It is now being used in various different conditions ranging from normal mid wifery to the treatment of cerebral hæmorrhage in premature infants

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[1] Medicine and Hygiene Geneva Oct 1, 1953.
[2] Jaulmes, C. Laborit H., Benitte A. *C R Acad Sci., Paris* 1953 234 37

It is in the field of surgery that artificial hibernation is thought in France to have its widest potential usefulness It enables the surgeon to carry out longer and more involved operations, for the risk of operative and postoperative shock is considerably reduced by hibernation In thoracic, cerebral, and cardiac surgery and in the treatment of shock from burns or severe trauma it has already proved of inestimable value

The wide use to which this measure is being put in France today is well illustrated by the recent annual meeting at the École de Puericulture in Paris, the papers included four on hibernation in pædiatrics Ill premature infants and children with various overwhelming infections, all gravely ill with an almost hopeless outlook of recovery, were treated by this method in addition to antibiotic therapy, a significant proportion recovered

This method is still regarded here with reserve, though there is understandable enthusiasm for its possibilities With further trial a more valid evaluation of its worth will be possible

D M

Medicine and the Law

Death in Hospital

AT a recent inquest at Rotherham[1] upon the victim of a traffic accident, the jury, while satisfied by the medical evidence that no possible lack of treatment at the hospital had been a contributory cause of death, recommended that immediate measures should be taken in future cases of injury They returned a verdict of accidental death The coroner observed that it seemed that a conflict of personalities among members of the hospital staff had perhaps created difficulty in deciding the measures to be taken

The deceased was knocked down by a car at 11 P M and was taken to hospital where he died $1\frac{1}{2}$ hours after the accident Dr X, the resident surgical officer, described the patient's injuries He told the coroner that, as it was an orthopædic case, Dr Y, the orthopædic registrar, was sent for He later found that Dr Y had not visited the ward "Had it been my patient," said Dr X, "I should have set up a plasma drip straight away" Dr Z, who took the message to Dr Y, said a radiographer had been sent for, he had outlined the case to Dr Y who had told him that, as it was a head injury and a surgical problem, the patient should be put to bed with a splint to the injury and he would see the case in the morning Dr Y's evidence was a denial that he had accepted the patient so far as the witness knew, the patient was in the care of the surgical ward, he himself could have done nothing except order a splint and await the result of the radiographic examination

The pathologist told the coroner in effect that a plasma drip would not have saved the patient "I honestly feel that a drip could possibly help as a remote chance, but it might help to kill"

The hospital management committee approved a month later, the report of a special subcommittee which had investigated the circumstances The findings were that all possible treatment had been given immediately, that there was no evidence that the conduct of the case was affected by any suggested personal differences existing between members of the staff, that the rules for casualty officers in such contingencies were in all respects adequate to secure immediate treatment, and that they had on this occasion been duly followed

If the facts of the case support the drawing of a moral, they may remind hospital managements of the necessity of making sure that the respective responsibilities of their officers are understood without risk of uncertainty

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[1] *Sheffield Telegraph* Sept 23

The Widdicombe File

IV ALL IN THE DAY'S WORK

DEAR HAWKE,

As one who profited by your instruction when you were in the path dept at St Cuthbert's, I was delighted to find you within a specimen's throw, so to speak

As you see, I've ended up in general practice—not really as a frustrated specialist, but because I like a bit of variety and the paths of hospital work seem to get narrower and narrower I've been lucky in joining a partnership (four of us now) in which we all want to provide the patients with as complete and comprehensive a service as we can Hence it's been suggested that I take over a small side room (in the surgery) as a lab and get it going to the mutual benefit of one and all Could I prevail on you to give me some help in the form of initial advice ?

Obviously, I shall have to cut out both time-consuming tests and expensive equipment On the other hand we ought to be able to undertake a limited range of direct pathological tests, which may save the patient a journey, tell us quickly what we want to know, and incidentally reduce the pressure on hospital outpatient departments and laboratories I'm very keen to do this, because it's one of the ways in which general practice can be kept an interesting and satisfying job instead of being allowed to degenerate into a daily grind Osler said that the true doctor should aim at having three rooms in his house well stocked—the library, the laboratory, and the nursery—books, balances, and bairns This letter is to tell you of my plans for the second room, I will say nothing of the first, and the inhabitants of the third speak for themselves, as you will soon find out when (as I hope) you pay us a visit

* * *

The room we have for a lab is small, but it has a sink and running water The local carpenter (a dignified craftsman with a large rhinophyma and a healthy distrust of the Welfare State) is fitting a bench, and we are having a daylight type strip light and a lamp on the bench for use with the microscope The tests I propose to do are as follows

Firstly, urine testing I plan to use the salicylsulphonic acid test for albumin and a 'Glucotest' tablet for sugar, on the ground of convenience and to avoid splashing boiling urine on the bench I have an Esbach's tube for the quantitative estimation of albumin For bile pigments I shall have strong nitric acid, and for acetone, ammonium sulphate, ammonia, and sodium nitroprusside We have a microscope for examining uncentrifuged urine for cells and casts

Secondly blood tests Genuine anæmia must surely be quite common in general practice, chiefly iron-deficient but a few pernicious We already have a Medical Research Council grey wedge hæmoglobinometer, which I'm pretty sure will justify its cost by the speed and accuracy with which one can do a number of estimations I have a technician's tray holding a rack of test-tubes with rubber bungs and numbered labels, each holding 4 ml of 0·04 % ammonia, together with a needle, pipettes for slides, and distilled water and acetone for cleaning the pipettes With everything at hand I find it takes about 90 seconds to take blood into the tube and make a film; then after the surgery, the samples can be put through the hæmoglobinometer at the rate of more than one a minute, the films are stained with Leishman and examined with the oil-immersion lens I feel that I ought to be able to recognise the appearances of iron-deficiency anæmia or P A If I am not sure about a film or come across anything unusual I would like to send nl of blood in a mixed oxalate bottle with an unstained ear for whatever tests you think necessary I don't pose to do red and white cell counts or other more borate tests as they take too long and in my hands uld be so inaccurate as to be useless The sedimentation te must surely be very useful in practice and I have ne Westergren tubes and bottles containing 0·4 ml 3·8% sodium citrate to which I add 1·6 ml of blood n I right in thinking that the only difficult thing about is test is to remember to read the result after the be has stood for one hour?

Thirdly, it seems to me that the Gregersen slide test occult blood in the stools should be simple and luable where there is a possibility of gastro intestinal eration or growth I have a tube graduated to 2·5 and nl., and the drill is

> Pour in glacial acetic acid to the first mark and dilute th distilled water to the second Shake in a benzidine t powder and let it dissolve Then bring a drop of the ution into contact with a spot of emulsified fæces on a de A blue colour developing within thirty seconds means ult blood—whatever the patient may or may not have ten in the way of meat

Am I right Sir? It all seems fairly easy for the res can be collected off a finger stall after rectal amination, or the patient can be told to bring a small mple in a bottle If reliable this should be a very lpful screening test for cases with gastro intestinal mptoms One positive test would show the need for rther investigations and a consultant's opinion, while ree negative tests would, I imagine be pretty good dence against ulceration or growth It should help us see that cancer of the stomach and bowel are diagnosed thout delay, and it should also help us to keep out of spital some of the people with abdominal symptoms se to anxiety and unhappiness. (You can't I suppose commend any handy lab test for these?)

Finally I have the reagents necessary for a Gram's ain with the idea of examining vaginal and urethral scharges for monilia or gonococci I also intend to look r trichomonas in freshly collected wet specimens which ust be more certain as well as more convenient than nding the specimen to the laboratory

'I have half a dozen 10 ml. all glass syringes for taking ood and I'd like to know whether my sterilisation chnique strikes you as all right—viz

> After use the syringes are washed in a detergent ("Tide") d then rinsed thoroughly first in tap water and then in stilled water When dry they are lubricated with liquid raffin and done up in test tubes with needles attached. hoose an auspicious moment and take them to the missus, ho pops them in the oven one hour at 160 C and they are ne

at is my sterile syringe service and it does not really ke up much time

* * *

'These are all the tests I think it worth my trying to dertake they are all simple, need little equipment and ke no longer than it would to make an appointment and ite a letter to the appropriate specialist or laboratory lthough the range is very limited it seems to me to cover large part of the *practitioner's day to day needs* nything more elaborate I would like to send along to m if you are willing; this is likely to include throat abs specimens of pus urine sputum and fæces for cteriological culture and control of antibiotic therapy; mples of blood for sugar and urea blood-counts glutinations and Wassermann tests. May I come to ur lab and collect a selection of bottles, swabs and rms?

'Anyway I look forward very much to meeting you ain,

Yours sincerely
BILL BREWER.

Parliament

Speech from the Throne

REFERENCES to housing and public health figured prominently in the Queen's Speech at the opening of the new parliamentary session on Nov 3 Her Majesty said that her Ministers would continue to encourage the building of houses and schools and would also stimulate a vigorous resumption of slum clearance Legislation would be introduced to facilitate the repair and improvement of existing houses both by local authorities and by private owners Legislation would be proposed to revise consolidate and extend the law on the safety, health and welfare of miners and quarrymen, to provide benefit for certain further cases of disablement from industrial diseases, to amend and consolidate the law relating to food and drugs, and to restrict night working in the baking industry The Road Traffic Acts were being attentively examined with a view to introducing further legislation to improve road safety and promote the orderly use of the roads.

In seconding the Address in reply to the Speech from the Throne Miss EDITH PITT said it was recognised that the success of the housing drive now made it possible to intensify slum clearance and encourage the repair and modernisation of some of the older types of houses. Health was the most important social service, and the treatment and prevention of tuberculosis presented a special challenge and a special opportunity—namely to eradicate this scourge The immediate problem was the need for more beds more nurses and more surgical facilities. It would help to make the most effective use of existing hospital beds if some kind of hostel or intermediate accommodation could be provided for those who needed only limited supervision and perhaps some nursing A recent survey in the Midlands had shown that 15–20% of the beds occupied came within this group

Sir WINSTON CHURCHILL, the Prime Minister emphasised that while new houses were being built at the rate *of 300,000 a year as many were mouldering into ruin* and a far larger number were denied the modern conveniences 2 250 000 houses were over a hundred years old and another 2,000,000 were between sixty and a hundred years old

Mr HAROLD MACMILLAN Minister of Housing and Local Government, said that the time had now come to take up the second part of the housing programme People living in old houses had just as much right to have their conditions improved as those moving into new houses In 1939 it was estimated that 6% of the population were living in unfit or overcrowded houses and although there was much to be done in the way of improving old houses and clearing slums, the national stock of houses and flats was now very nearly equal to the number of separate families 2 million accommodation units had been provided since the end of the war during which some 250 000 houses were destroyed The answer to the question why the housing lists were still so large was twofold First of all higher standards of living had created a demand for a higher standard of housing Secondly there were now far more single people and old people and there were more young married couples most of them wanting a home of their own As to the slums the National Housing and Town Planning Council estimated that about 500 000 dwellings could be classed in this category; there might be even more He had already had informal talks with the local authorities which would be asked to put forward programmes for dealing with the slums

Mr ANEURIN BEVAN said that the Government had brought forward a scheme which had the maximum of political odium and would have the minimum of physical results Not only slum clearance and reconditioning but all rent-restricted houses must eventually become the responsibility of local authorities. Under this system the houses that would be first repaired would not be those which under the Government's formula became profitable for landlords to repair, but those that needed repair first Even if the Government's formula was effective in getting all the repairs carried out it would mean a diversion of resources from other operations

Future of Hospital Registrars

On the motion for the adjournment in the House of Commons on Nov 6, Mr HORACE KING drew attention to the employment problems of hospital registrars He recalled that when the National Health Service began many doctors took up posts as registrars in the belief that the consultant service was to be expanded In fact it had been expanded to a remarkable extent But it had been impossible to foresee how great the expansion would be, and in 1951 it was discovered that there were more registrars than the health service could absorb In the long run, he thought, everyone agreed that Mr Bevan had made a wise decision when he decided to cut the intake of registrars and to approximate the intake to the number of consultant posts likely to become vacant from year to year But Mr King was concerned with the 300-400 senior registrars who had already entered this apprenticeship and who now found it difficult to obtain posts of any kind

When the cut was made the then Minister of Health had said that registrars who failed to obtain consultant posts need not be alarmed because they could go either into the Colonial Service or into general practice But Mr King pointed out that though doctors were undoubtedly needed overseas these posts were more suitable for younger men The men he had in mind were now 35 to 40 years of age, mostly ex-Servicemen with family responsibilities, who ought to be settling down, not starting a career in a new world On the other hand, when a registrar's period of hospital service came to an abrupt end and he tried to get into general practice his position became really alarming Mr King knew of men with excellent academic qualifications who had not even got on to the short list of candidates for a vacant post

Vacancies, he understood, were filled in the first place by a joint committee consisting of members of the health executive and the local medical committee The former might be laymen the latter were entirely members of the medical profession This joint committee prepared a short list, sometimes interviewed the candidates, sometimes did not On this local joint committee local doctors could exercise the fullest influence over the laymen The short list then went to the Medical Practices Committee, a national body consisting entirely of doctors, which finally made the appointment If a wrong was being done by the health service to the registrars, it was being done by the members of the medical profession Polarity had grown up between the general practitioners and the consultant service He hoped that the gap would be bridged, it would be a pity if in the meantime the general practitioners were hurting these hospital registrars because of their emotional reactions to being kept out of consultant work in general hospitals He appealed through the Minister to the medical profession on behalf of this group of deserving and able men The solution of the problem lay largely in the hands of the profession, this dominated the Minister's committee which, independent of any control, filled partnership and assistant posts as they became vacant

Miss PATRICIA HORNSBY-SMITH, parliamentary secretary to the Ministry of Health, agreed that more doctors had entered the senior-registrar grade than could be absorbed into consultant posts It had now been agreed with the profession that there should be an intake of approximately 270 new senior registrars each year They had met the inflation in the number of senior registrars by increasing the number of consultant posts, and by temporarily extending some of the senior-registrar posts to give those men a fair opportunity to obtain consultant posts

The number of senior registrars in the early years of training was now closely in line with the number agreed with the profession The number in the later stages of training was still in excess of the vacancies, and there was a limit to the vacancies which could be made for them But those in the senior-registrar group had had a greater opportunity to find specialist vacancies in the past five years than they had before, because of the increased number of vacancies, or than they were likely to have in the future The suggestion that consulta were staying on longer was not borne out by the fa The number of consultants who were 65 and over were still in the service in 1950 was 120, in 1951 and in 1952, 78

The largest problem was undoubtedly the classification of registrars It was never thought all those who took registrar posts could become sp The development of medical treatment and of the pital service generally had called for many more and there was a grave shortage of this grade in areas The remedies must include an increase in time and part-time registrars For the part registrar they must look to the general particularly those who had just started in practice were prepared to do part-time work while their practice The increased need for full time in the hospital service meant that to the registrar's appointment was a normal step in the part of his career before going into public health or to the Colonies Many of them would have to into medical posts outside the hospitals

As to the suggestion that there was di against registrars when they attempted to get general practice, Miss Hornsby-Smith thought too much emphasis had been put on the adv vacancy, which was usually for a single-handed prac often vacated by a practitioner of long-standing had a fairly substantial list It was not surprising preference was often given to the man who had general-practitioner experience But 60% of the for general practice were in partnerships. It was c for our doctors to practise in partnership and she this custom would not lessen Registrars must beyond the advertised vacancies and realise that larger field lay in other appointments For in in March and April this year, 154 new partners taken into partnership, 238 assistants became with their principals, but there were only 24 a vacancies A registrar's first steps in general pra would more advisably be taken in a partnership having obtained general-practice experience, he be a strong candidate for a single handed p It was usual and reasonable for the committees to men with general-practice experience for these vac and it was a little unreasonable for an ex registr expect to step straight into a large, advertised handed practice There was no evidence that d were discriminating in any way against ex regis many of whom had obtained posts

QUESTION TIME

Masks Against Fog

Mr SOMERVILLE HASTINGS asked the Minister of what researches had been made to determine how much sulphur oxides and other gaseous contents of fog were from inspired air by the use of a dry gauze mask Dr P STROSS asked a similar question —Mr IAIN MACLEOD There has been extensive research, both here and abroad protection from the toxic solid and gaseous contents of different conditions Respirators to achieve this have known for many years, they are of rather elaborate types, something like those used in the Forces. But problem of the "smog" is that of persons—and partic old persons—suffering from weaknesses of the lungs or as last winter showed, and further research is need determine what respirators could be safely worn by people for long periods This is going on actively amongst outpatients of a large hospital As to surgical gauze ma chiffon scarves, I am advised that they would be of littl no value in absorbing the toxic gases, although like any comparable form of improvised protection they would some of the solid particles in a fog

Byssinosis Benefits

In answer to a question, Mr R H TURTON, Mini Pensions and National Insurance, said that up to Oct 1953, the number of claims under the pneumoc and byssinosis benefit scheme in respect of byssinosis about 100 for disablement and 25 for death Awards 85 and 21 respectively

In England Now

Running Commentary by Peripatetic Correspondents

'THERE'S nothin' so queer as scent cept a woman! d Mr Jorrocks and the more I watch my blood unds manhunting the more I share his view, at least on the first half of the comparison

Having once dabbled in the mystics of E.N.T. I ought I understood the physiology of smelling When untryside offered long days of hunting foxes, hares, d otters familiarity with scent bred that cocksure ntempt which traditionally precedes a fall.

The day we started keeping bloodhounds marked the astening descent to true humility It soon became parent during training that the hounds were teaching far more than we could teach them and when the bble of our false pride was well and truly pricked we out to recapture the atavistic echo of a sensory echanism long surrendered by Man in his evolutionary urse of differentiation.

Bloodhounds detect colder scents than probably any her animal because over a thousand years of selective eding have been focused on their noses But do they ssess a wider spectrum for olfactory stimuli or have y merely a more delicate sensory appreciation? hink that they have both Certainly they can recognise ells beyond the olfactory range of man just as the s of dogs can register notes far above man's upper lt of hearing Even when a human being picks up pungent smell of a fox on a still autumn morning is probably not the scent which the foxhounds run d I have grovelled in vain on the ground to try and pture a whiff of the scent of man which a bloodhound ns so confidently So, too, they have an amazing licacy of appreciation of faint odours. Many hounds ve hunted lines several days cold, and I have even tched my old bitch dig the kit of victims of a mountain ident from the snow after 47 days; but perhaps persistence of scent is one of its vagaries

Although hounds must live in a world of smells, they ve a well-developed discrimination even to differen ting between individuals of one species Just as young thounds will change on to a fresh fox so young odhounds will change on to a fresh human quarry til training has impressed upon them that they must k to one scent There is also some scent memory chanism which carries the hounds over checks and pires them to cast for themselves and pick up the trail in without changing. This mental concentration imposes oticeable strain on hounds and they show fatigue far excess of the physical effort involved

When the snows are thick it is quite instructive to tch a bloodhound bury his nose into the quarry's tprints snuffle loudly, and then bound forward to eat the process On the other hand a fresh cross wind l cause the hound to run the line some ten to forty ds parallel with the quarry's path and in the still n of evening the drift of cool air down the fellside l lift the head of a bloodhound to mark a man even arter of a mile uphill

used to wonder whether a man's personal scent was ained after death or whether it was replaced by the erie cadaver smell with which we are all familiar ving watched my own hounds locating bodies I eve that the personal scent lingers long after death m such morbid contemplations it might be more reshing to reflect upon the second half of Mr Jorrocks's mparison though possibly more ungallant

* * *

It was a bad mistake for a young doctor in a new ctice: the whole village must now know that I have fused two easily distinguishable growths. While the tman and I were admiring each other's allotments ointed to his parsnips and remarked on the strength l vigour of his celery It was doubly unfortunate that was the postman, for the story was round the village h the morning delivery

For a time I didn't dare to show my face in my den; but grass and hedges will grow and eventually ad to emerge I started by cutting back the hawthorn ge. As often happens when one is engaged on routine repetitive work my thoughts began to wander and I found myself considering the perennial problem of the industrial medical officer—how to persuade the workmen to wear their protective clothing how to convince them that accidents will happen even to them, how to eradicate the juvenile fantasy that it is cissy to put on goggles, gloves, or aprons Just then my friend the postman came down the road "You want gloves for that job" he said 'Those thorns can give you a nasty hand'

* * *

On Friday morning I turn first to this column and after that to the Letters to the Editor There I am always prepared for a recurring irritation About a third of the letters begin I have read with interest or 'I am interested : and I can't think why Does not the correspondent realise that it is superfluous to announce his 'interest'? The mere fact of his putting pen to paper shows that. It might of course be appropriate to observe that he has read with amusement admiration enjoyment, approval, surprise consternation contempt, disgust, regret sorrow, dismay, or any one of a hundred expressions of his emotion But interest! His communication would be all the better for the omission of this presumably apologetic explanation of his request for the usual valuable space.

* * *

Some years ago I was rash enough to buy a book. I forget what it was—something to do with first-aid, probably, or the care and maintenance of the golden hamster Anyway I asked them to charge it, and from that moment dates my inferiority complex. They have got it into their heads that I am a good prospect, an easy touch and not a week passes but they send me a catalogue of *New and Forthcoming Scientific Books* Every fourth or fifth week I receive a catalogue (slightly foxed) of *Old and Rare Scientific Books*, and every two or three months—so bewildering is our English climate—there arrives the *Autumn List of Scientific Books*

It is these catalogues that depress me, particularly the mathematical section These chaps don't fiddle around with experiments They *know* It is impossible to read the brief chapter headings without a stirring of the emotions. The Hopf Invariant Fibre Spaces; the Hurewicz Theorems how they would reverberate in the mind of the reader! Or again Some Fundamental Properties of Noetherian Rings, Residue Rings and Rings of Quotients; A New List of P multiplied Laplace Transforms these are the very stuff of science, the life's blood of the future

When I have read through the catalogues I often go along to the animal house and look at all those rabbits and feel quite low in my mind. Last week I felt so badly about it I went out and bought another book.

* * *

I have always been fascinated by reports of treatment by hypnosis, but Sheila, my wife is a confirmed sceptic.

Both of us have a phobia of spiders. I never touch the things if I can avoid it but luckily Philip our four-year-old son likes spiders (particularly the big ones) and will keep them clasped firmly in his fist until persuaded to put them in the garden

I suppose it was because Philip showed such disregard for them that I decided it was time to overcome Sheila's fears. One night, just as we were going to sleep, I told her in my most compelling tones using the most modern abreactive technique that she could see large and horrible spiders everywhere, great enormous monsters all over the room, but never again would she be frightened by these lovable and handsome arachnids. I was still saying this when slumber overtook me

The next night we saw a huge spider I went straight to it, picked it up played with it in my hands and threw it out of the window I looked round with the light of victory in my eyes and saw that Sheila had fainted

* * *

I have never entertained any strong views on geriatrics or my geriatric colleagues but now all that has changed I overheard a nurse trying to explain to a confused 80 year-old that she was safe in hospital. In hospital? the old lady croaked incredulously The nurse nodded in triumph 'Oh! is that all? Thank goodness for that. I thought I was in hell'

Letters to the Editor

ETHICAL STANDARDS IN CLINICAL RESEARCH

SIR,—I am very glad that Dr Fisher has called attention last week (p 993) to the increasingly common failure to observe one of the primary rules of medical ethics

The privileged position which doctors hold in society depends entirely on the trust which people have in the purity of their motives This is stated explicitly in the international code adopted by the World Medical Association in 1949 "Under no circumstances is a doctor permitted to do anything which would weaken the physical or mental resistance of a human being except from strictly therapeutic or prophylactic indications imposed in the interests of the patient" There is no justification here for risking an injury to an individual for the possible benefit to other people, as enunciated by Dr Holt as his guiding principle Such a rule would open the door wide to perversions of practice, even such as were inflicted by Nazi doctors on concentration-camp prisoners The magnitude and crudity of their "experiments" must not be allowed to blunt sensitivity to breaches of the medical ethic made on a smaller scale and with greater plausibility Of this nature are experiments performed upon condemned criminals, with or without the victim's consent, upon conscientious objectors to military service, upon persons with chronic mental illness or deficiency or incurable disease of any kind, and all procedures, whether therapeutic in intent or not, which are not designed with the sole intention of improving the lot of the individual upon whom they are performed Only one exception can be allowed—i e, when the experimental subject is an adult whose judgment is not impaired and who freely gives his consent No child must ever be the subject of such an experiment

I could quote many examples, published without comment or attempted justification in the medical press of English-speaking countries, of the failure to observe this rule Here are three, all quite recent

(1) Potentially harmful doses of ageno given to children in an orphanage, in order to see whether such doses were toxic

(2) The use of patients with incurable cerebral tumours as experimental subjects for finding out whether intrathecal aureomycin was injurious the experiments involved multiple lumbar punctures

(3) Attempts to reproduce dangerous syncopal attacks in a child in order to obtain graphic records

It is clear that the assumption by doctors of scientific methods and techniques calls for critical examination of the uses to which these methods are put The scientific material of the clinical research worker is human life Some discussion of the issues involved took place in a symposium at the Chicago Medical School in 1952[1]

I should like to see a resumption of the practice by which all doctors upon qualification were required to make a declaration of adherence to the medical ethic There is need for a revised, more simple form of the Hippocratic oath, relevant to the circumstances of the 20th century For some time the ethics subcommittee of the Medical Association for Prevention of War has been occupied with such a revision, and I give, for the sake of discussion, the tentative and interim results of this attempt

At the time of being admitted to the medical profession, I swear to regard my duty as a doctor as overriding all other obligations, in particular I will not allow considerations of race or nationality, nor my own personal profit, to interfere with my performanc that duty, namely

(1) To promote, with all the means at my comma civilised standards of life and health throug the world

(2) To direct all my work to the preservation of and the relief of suffering, and under no circ stances whatever to use my medical know to harm any person, nor take part in any ex ment involving risk of injury, without myself of the understanding and freely g consent of an adult subject, nor without consu my colleagues upon the value and necessity such an experiment

(3) To coöperate in every way possible with doc and health-workers in all countries both in of peace and in time of war to work at all for the preservation of peace

(4) To communicate freely to all doctors an coveries which I believe myself to have concerning the nature, cure, or preventio disease

(5) Never to abuse the position of privilege in my profession has placed me, to respect confidences of patients but not to allow su to endanger the health or lives of others

I will be ready, if need be, to sacrifice my health, or life, rather than be unfaithful to this oath

Bickley Kent DUNCAN LE

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[1] See *Science* 1953 117, 205

INCISION FOR ACUTE APPENDICITIS

SIR,—The report by Mr Ewing and Mr W (Oct 24) of one case of acute appendicitis is conv proof that this humble malady has not passed unn by the Postgraduate Medical School, but some d may justifiably remain as to whether the complica described would have been averted by a muscle-spli incision

They advise this incision in "all cases in which appendicitis is diagnosed," and add that the param incision should not be made a cloak for slovenly diag Is it not time that our teaching schools cease encourage the hypocrisy implied by "a con diagnosis of appendicitis"? Space precludes a descr of the 21 different abdominal catastrophes which I personally mistaken for acute appendicitis, but case report may serve to emphasise the stresses to a slovenly diagnostician may be exposed

A lady of 52 was admitted with a ten-day history of abdominal pain, she had a tender mass in the right ili a temperature of 101 6°F, and a white cell count of per c mm She did not long survive an incision which to shortest possible route into a leaking aneurysm of abdominal aorta

The criss crossing gridiron incision cannot be d satisfactorily, it frequently becomes infected, and gives very inadequate access to the pelvis and no at all to the rest of the abdomen It remains th incision in advanced pregnancy, and for cases in w tenderness is maximal in the flank It is satisfactor young men with mild symptoms

Battle's incision is very rarely followed by he because divarication of the recti, which weakens midline and paramedian wounds, crowds the m into the lateral part of the rectus sheath

The unrivalled exposure afforded by the param incision makes it, on balance, the most satisf "standard" approach If it is made well below umbilicus (in young women an obvious hollow marks spot), quite a short incision gives excellent acce pelvis where a hidden collection of pus can easi overlooked When an abscess is present in the right fossa, the rest of the abdomen can be packed off b the exploring finger releases a gush of pus A la llows in a small percentage of cases but the repair lvised by Cattell has robbed the operation of much of s difficulty

The poor cosmetic result of the paramedian incision is rtly concealed when the patient is examined on a couch the erect position an ugly transverse fold appears at e upper limit of the scar For this reason I have taken using the *Pfannenstiel* or *bikini" incision for* xploring the lower abdomen in girls whose face and gure may play a part in their fortune It gives very od access, is immune from hernia and is much ppreciated

Barnet General Hospital. V J DOWNIE

SIR,—If I say that the plea of Mr Ewing and r Monro for the use of the gridiron incision in pendicitis is to me what Mr Punch calls ' another impse of the obvious, I am not unmindful that many rgeons still make large paramedian holes and that the minder is salutary Many think that one cannot al with the appendix through a gridiron incision in ung children and even in babies, whereas the procedure not nearly as difficult as it in theory might appear have pointed out elsewhere[1] the advantage of this cision in dealing with long standing recurrent abdominal pain in children where the diagnosis is not firm it where parents are kept in continual suspense lest e next attack may be a fulminating appendicitis. By e time it is decided that intervention is necessary any sion in any other part of the abdomen will almost rtainly have manifested itself and through a gridiron cision one can see and remove the appendix examine the esentery *for adenitis and withdraw enough small bowel* exclude a Meckel s diverticulum These are the three kely organic causes of such recurrent pain when the dney has been excluded

The morbid result described by Ewing and Monro llowing a paramedian incision reminds me that someone ice said that no-one who had had a paramedian incision er played on the centre court at Wimbledon It may an overstatement but the sequelæ to large laparo mies especially in the presence of sepsis, make me ink that any exception is likely to be a rarity

On Mr Shemilt s dictum (Oct. 31) that the abdomen ould never be drained in appendicitis I will confine yself to parliamentary language and only register ief as he also in time will certainly if he persists with ch practice in children It is the drain that is left in o long that does harm

London W 1 CHARLES DONALD

SIR,—Mr Shemilt s letter moves me to support a plea for Battle s maligned incision It has served e well for forty years I do not recommend it for ening an abscess or for very fat patients, and I prefer oblique muscle-cutting incision for the high lying trocæcal appendix

With Battle s incision the nerves are clearly seen and ould not be cut Their distribution seldom conforms the diagrams in anatomy books Caution must be ed in extending the incision upwards but, after ntrolling the deep epigastric vessels it can be carried wn to give excellent access to the pelvis Hernia is re after Battle s incision and my impression is that it is ore often seen after McBurney s

Colt and Morrison[2] in an inquiry into the relationship tween the death rate after operation for acute appendi itis and the incision used found that much the west mortality occurs with the Battle incision Their ticle is worth studying

Northampton. C C HOLMAN

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[1] *Practitioner* 1952 168 41
[2] Colt G H., Morrison M M *Brit. J Surg* 1932 20 107

THERAPY OF DIARRHŒA IN CHOLERA

SIR,—The diarrhœa and vomiting of cholera lead rapidly to a great loss of body fluid and electrolytes and ultimately to progressive shock which is often irreversible and fatal During the last few decades workers on cholera have been trying every available remedy to check this diarrhœa, but without any appreciable success The sulpha drugs[1-3] and the antibiotics chloramphenicol[4 5] terramycin,[6-8] and aureomycin[9 10] have little or no effect in checking the diarrhœa or in reducing the mortality rate of cholera, although the antibiotics can render the stools bacteriologically negative Consequently the present tendency in cholera therapy is to disregard the diarrhœa and to concentrate on the replacement of fluid and electrolytes.[9 11]

During the severe epidemic of 1953 in Calcutta the cholera patients in my ward were given by mouth the crude juice from the leaf of a common plant of Bengal called pathorchur " (*Coleus aromaticus*) a short green plant about 2 ft high with thick crenate leaves giving off a camphor like odour (see figure) The juice from the leaf is a greenish fluid with a pleasant taste and smell and without any deleterious effect on any physiological system The dosage consisted of the following hourly doses: 1st dose 4 teaspoonfuls 2nd and 3rd doses 2 teaspoonfuls each If the diarrhœa continued after eight hours on the first day the doses were repeated in the evening On subsequent days the above doses were repeated unless there was constipation. Every 6th case in order of admission was tested as a control. The 40 controls were not given any leaf juice but the routine treatment of shock and other complications were just the same as in the treated cases In addition, the control cases received four doses daily of a routine suspension containing kaolin (gr 30) and bismuth carbonate (gr 20) in each dose The following results were obtained

(1) Of 200 treated cases the diarrhœa was checked within twenty four hours in 40% within forty-eight hours in 74%. and within seventy two hours in 92 5% Of 40 controls the diarrhœa was spontaneously checked within twenty four hours in 5% within forty-eight hours in 12 5%, and within seventy two hours in 30%

(2) Stool cultures showed a peculiarity—i e. rough colonies of the vibrio appeared comparatively early in the second culture after twenty four hours leaf juice therapy The proportion of rough colonies to smooth continued to increase in the successive cultures the smooth colonies being scanty

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1 Lahiri S C. *Brit. med J* 1951 i 600
2 Chaudhuri, A. K. R., Chaudhury A., Chadha V N *Antiseptic,* 1952 49, 417
3 Konar N R. Sen Gupta, A N., Baksh, E. *Calcutta med. J* 1953, 50 412
4 Gauld R. L., Schlingman, A. S Jackson, F B Baston H C Cambell C C. *J Hyg* 1949 57 610
5 Chaudhuri, R. N., Ghosal, S., Rai Chaudhuri, M N *Indian med Gaz.* 1950, 85 389
6 Chaudhuri, R. N., Ghosal, S C., Mondol A Chakravarty N K. *Ibid,* 1953 87 135
Das, A, Ghosal, S., Gupta S. K., Chaudhuri, R. N *Ibid* 1951 86, 437
8 Konar N R., Sengupta, A N *Ibid* p 469
9 Das, A Ghosal, S. C., Mondol, H., Gupta, S K. *J Indian med Ass.* 1953 22 468
10 Seal, S C., Ghosal S C Ghosh, M. M *Indian med Gaz* 1951 86, 257
11 McRobert G *Practitioner* 1952 169 470

Letters to the Editor

ETHICAL STANDARDS IN CLINICAL RESEARCH

SIR,—I am very glad that Dr Fisher has called attention last week (p 993) to the increasingly common failure to observe one of the primary rules of medical ethics

The privileged position which doctors hold in society depends entirely on the trust which people have in the purity of their motives This is stated explicitly in the international code adopted by the World Medical Association in 1949 "Under no circumstances is a doctor permitted to do anything which would weaken the physical or mental resistance of a human being except from strictly therapeutic or prophylactic indications imposed in the interests of the patient" There is no justification here for risking an injury to an individual for the possible benefit to other people, as enunciated by Dr Holt as his guiding principle Such a rule would open the door wide to perversions of practice, even such as were inflicted by Nazi doctors on concentration-camp prisoners The magnitude and crudity of their "experiments" must not be allowed to blunt sensitivity to breaches of the medical ethic made on a smaller scale and with greater plausibility Of this nature are experiments performed upon condemned criminals, with or without the victim's consent upon conscientious objectors to military service, upon persons with chronic mental illness or deficiency or incurable disease of any kind, and all procedures, whether therapeutic in intent or not, which are not designed with the sole intention of improving the lot of the individual upon whom they are performed Only one exception can be allowed—i e, when the experimental subject is an adult whose judgment is not impaired and who freely gives his consent No child must ever be the subject of such an experiment

I could quote many examples, published without comment or attempted justification in the medical press of English-speaking countries, of the failure to observe this rule Here are three, all quite recent

(1) Potentially harmful doses of agene given to children in an orphanage, in order to see whether such doses were toxic

(2) The use of patients with incurable cerebral tumours as experimental subjects for finding out whether intrathecal aureomycin was injurious the experiments involved multiple lumbar punctures

(3) Attempts to reproduce dangerous syncopal attacks in a child in order to obtain graphic records

It is clear that the assumption by doctors of scientific methods and techniques calls for critical examination of the uses to which these methods are put The scientific material of the clinical research worker is human life Some discussion of the issues involved took place in a symposium at the Chicago Medical School in 1952[1]

I should like to see a resumption of the practice by which all doctors upon qualification were required to make a declaration of adherence to the medical ethic There is need for a revised, more simple form of the Hippocratic oath, relevant to the circumstances of the 20th century For some time the ethics subcommittee of the Medical Association for Prevention of War has been occupied with such a revision, and I give, for the sake of discussion, the tentative and interim results of this attempt

'At the time of being admitted to the medical profession I swear to regard my duty as a doctor as over-riding all other obligations, in particular, I will not allow considerations of race or nationality, nor my own personal profit, to interfere with my performance of that duty, namely

(1) To promote, with all the means at my command, civilised standards of life and health throughout the world

(2) To direct all my work to the preservation of life and the relief of suffering, and under no circumstances whatever to use my medical knowledge to harm any person, nor take part in any experiment involving risk of injury, without assuring myself of the understanding and freely given consent of an adult subject, nor without consulting my colleagues upon the value and necessity for such an experiment

(3) To cooperate in every way possible with doctors and health-workers in all countries both in time of peace and in time of war to work at all times for the preservation of peace

(4) To communicate freely to all doctors any discoveries which I believe myself to have made concerning the nature, cure, or prevention of disease

(5) Never to abuse the position of privilege in which my profession has placed me, to respect the confidences of patients but not to allow secrets to endanger the health or lives of others.

I will be ready, if need be, to sacrifice my security, health, or life, rather than be unfaithful to this oath."

Bickley, Kent. DUNCAN LEY

INCISION FOR ACUTE APPENDICITIS

SIR,—The report by Mr Ewing and Mr Moore (Oct 24) of one case of acute appendicitis is convinc proof that this humble malady has not passed unnoti by the Postgraduate Medical School, but some do may justifiably remain as to whether the complicati described would have been averted by a muscle splitting incision

They advise this incision in "all cases in which ac appendicitis is diagnosed," and add that the paramedi incision should not be made a cloak for slovenly diagno Is it not time that our teaching schools ceased encourage the hypocrisy implied by "a confi diagnosis of appendicitis"? Space precludes a descript of the 21 different abdominal catastrophes which I ha personally mistaken for acute appendicitis, but case-report may serve to emphasise the stresses to wh a slovenly diagnostician may be exposed

A lady of 52 was admitted with a ten day history of lo abdominal pain; she had a tender mass in the right iliac fo a temperature of 101 6°F, and a white cell count of 23,0 per c mm She did not long survive an incision which took the shortest possible route into a leaking aneurysm of the abdominal aorta

The criss crossing gridiron incision cannot be drain satisfactorily, it frequently becomes infected, and gives very inadequate access to the pelvis and no acc at all to the rest of the abdomen It remains the incision in advanced pregnancy, and for cases in wh tenderness is maximal in the flank It is satisfactory young men with mild symptoms

Battle's incision is very rarely followed by her because divarication of the recti, which weakens midline and paramedian wounds, crowds the mu into the lateral part of the rectus sheath

The unrivalled exposure afforded by the paramedi incision makes it, on balance, the most satisfac "standard" approach If it is made well below umbilicus (in young women an obvious hollow mark spot), quite a short incision gives excellent access to pelvis, where a hidden collection of pus can easily overlooked When an abscess is present in the right i fossa, the rest of the abdomen can be packed off b the exploring finger releases a gush of pus A h

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1 See *Science* 1953 117, 205

ws in a small percentage of cases but the repair sed by Cattell has robbed the operation of much of ifficulty

he poor cosmetic result of the paramedian incision is ly concealed when the patient is examined on a couch he erect position an ugly transverse fold appears at upper limit of the scar For this reason I have taken using the Pfannenstiel or bikini' incision for oring the lower abdomen in girls whose face and re may play a part in their fortune It gives very l access is immune from hernia and is much reciated

urnet General Hospital. V J DOWNIE

m,—If I say that the plea of Mr Ewing and Monro for the use of the gridiron incision in endicitis is to me what Mr Punch calls 'another ipse of the obvious I am not unmindful that many geons still make large paramedian holes and that the inder is salutary Many think that one cannot l with the appendix through a gridiron incision in ng children and even in babies, whereas the procedure ot nearly as difficult as it in theory might appear ave pointed out elsewhere[1] the advantage of this mon in dealing with long standing recurrent abdo al pain in children where the diagnosis is not firm where parents are kept in continual suspense lest next attack may be a fulminating appendicitis. By time it is decided that intervention is necessary any on in any other part of the abdomen will almost ainly have manifested itself, and through a gridiron sion one can see and remove the appendix examine the entery for *adenitis, and withdraw enough small bowel* xclude a Meckel s diverticulum These are the three ly organic causes of such recurrent pain when the ney has been excluded

he morbid result described by Ewing and Monro owing a paramedian incision reminds me that someone e said that no-one who had had a paramedian incision r played on the centre court at Wimbledon It may an overstatement but the sequelæ to large laparo ies especially in the presence of sepsis make me k that any exception is likely to be a rarity

On Mr Shemilt s dictum (Oct 31) that the abdomen uld never be drained in appendicitis I will confine self to parliamentary language and only register f as he also in time will certainly if he persists with h practice in children It is the drain that is left in long that does harm

ondon, W 1 CHARLES DONALD

IR,—Mr Shemilt s letter moves me to support plea for Battle s maligned incision It has served well for forty years I do not recommend it for ning an abscess or for very fat patients, and I prefer oblique muscle cutting incision for the high lying rocæcal appendix

With Battle s incision the nerves are clearly seen and ould not be cut Their distribution seldom conforms the diagrams in anatomy books Caution must be d in extending the incision upwards but, after ntrolling the deep epigastric vessels it can be carried wn to give excellent access to the pelvis Hernia is e after Battle s incision, and my impression is that it is re often seen after McBurney s.

Colt and Morrison[2] in an inquiry into the relationship tween the death rate after operation for acute appendi is and the incision used found that much the est mortality occurs with the Battle incision Their ticle is worth studying

Northampton. C C HOLMAN

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[1] Practitioner 1952 168 41
[2] Colt G H Morrison M M *Brit J Surg* 1932 20 197

THERAPY OF DIARRHŒA IN CHOLERA

SIR,—The diarrhœa and vomiting of cholera lead rapidly to a great loss of body fluid and electrolytes and ultimately to progressive shock which is often irreversible and fatal During the last few decades workers on cholera have been trying every available remedy to check this diarrhœa, but without any appreciable success. The sulpha drugs,[1-3] and the antibiotics chloramphenicol [4-6] terramycin [6-9] and aureomycin [9,10] have little or no effect in checking the diarrhœa or in reducing the mortality rate of cholera, although the antibiotics can render the stools bacteriologically negative Consequently the present tendency in cholera therapy is to disregard the diarrhœa and to concentrate on the replacement of fluid and electrolytes [9,11]

During the severe epidemic of 1953 in Calcutta the cholera patients in my ward were given by mouth the crude juice from the leaf of a common plant of Bengal called 'pathorchur' (*Coleus aromaticus*), a short green plant about 2 ft high with thick crenate leaves giving off a camphor like odour (see figure) The juice from the *leaf* is a greenish fluid with a pleasant taste and smell and without any deleterious effect on any physiological system The dosage consisted of the following hourly doses 1st dose, 4 teaspoonfuls 2nd and 3rd doses 2 teaspoonfuls each If the diarrhœa continued after eight hours on the first day the doses were repeated in the evening On subsequent days the above doses were repeated unless there was constipation Every 6th case in order of admission was tested as a control The 40 controls were not given any leaf juice but the routine treatment of shock and other complications were just the same as in the treated cases In addition, the control cases received four doses daily of a routine suspension containing kaolin (gr 30) and bismuth carbonate (gr 20) in each dose. The following results were obtained

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1 Lahiri, S. C. *Brit med J* 1951 i 500
2 Chaudhuri, A K. R., Chaudhury A., Chadha, V N *Antiseptic* 1952 49, 717
3 Konar N R., Sen Gupta, A. N Baksh E. *Calcutta med. J* 1953, 50 217
4 Gauld R. L., Schlingman, A. S., Jackson E. B., Beaton H C., Cambell, C. C *J Bact.* 1949 57 510
5 Chaudhuri, R. N Ghosal, S., Rai Chaudhuri M N *Indian med. Gaz.* 1950, 85 398
6 Chaudhuri R. N., Ghosal, S C., Mondol, A Chakravarty N K *Ibid* 1953, 87 435
7 Das, A., Ghosal S., Gupta S K., Chaudhuri R. N *Ibid* 1951 86, 437
8 Konar N R., Sengupta, A N *Ibid* p 469
9 Das A., Ghosal S C., Mondol H., Gupta, S K. *J Indian med Ass.* 1953 22, 268
10 Seal, S C., Ghosal, S. C., Ghosh M M *Indian med Gaz.* 1951 86, 387
11 McRobert G *Practitioner* 1952 169 430

or absent in the fifth or sixth culture In the controls smooth colonies preponderated up to the twelfth culture

(3) The mortality rate was 8 5% (17 cases out of 200) with caf juice therapy 20% (8 cases out of 40) among the control cases, and 19 7% (215 cases out of 1093) among all the patients with cholera admitted to the ward

This treatment of diarrhœa, combined with the treatment of vomiting with 'Avomine,' plus the use of antihistamines and vitamin C for their preventive and curative effects against uræmia,[12] made it possible to dispense with parenteral and intravenous injection of fluid in a substantial number of patients who would otherwise have required this

Chittaranjan Hospital
Calcutta

HEMENDRA NATH CHATTERJEE

DRIED BONES

SIR,—I hesitate to intrude on your columns with so small a matter, but surely Dr Davies and Dr Harvey (Oct 24) are maligning the Far East in fathering upon it their anthrax-infected bones (even though they were shipped from somewhere East of Suez) East is East, Near East is the Levant, Middle East Babylonia, and the Far East Malaysia and the China Seas These bones came from India and Pakistan, which are no sort of East on this reckoning One of the minor snags of the partition is that it has left us with no convenient name for the subcontinent, but to misuse the term Far East is no answer to the problem

Postgraduate Medical School of
London, W 12

BERNARD LENNOX

ASPHYXIA IN THE NEWBORN

SIR,—Professor Pask (Oct 31) quite properly draws attention to the defects in the explanation and diagram in my letter of Oct 17, and I am sorry that he feels he has been misquoted The details of the apparatus could be only briefly described in a letter, so perhaps I may add some further explanation

The endotracheal tube used most often is a McGill size 00 The needles are those supplied by the Canadian Red Cross and are somewhat larger than the needle in the standard giving set Rebreathing in the anæsthetic sense—namely, to conserve an anæsthetic agent—is not required The infant does not rebreathe to any great extent, for the supply of oxygen is more than adequate Sometimes the fingers of the glove have been taped off and the glove attached to a branch piece of suitable diameter, and then rebreathing was really taking place However, most often the setting of the oxygen supply is such as to inflate the glove partly This works well as an indicator of spontaneous respiration, as well as being all that is necessary for gentle inflation It should be remembered that an infant face mask is manufactured and widely used It fits the standard Boyle's machine and in the resuscitation of infants it is commonly used with the adult rebreathing bag

My diagram showed a tube leading to an oxygen supply but the oxygen is not connected directly two release needles intervene and a reducing valve supplies oxygen at a low pressure A water manometer is not used, for I think that there is a real risk that the first (and most important) spontaneous inspiration might result in the aspiration of water The endotracheal tube is never a tight fit in the infant trachea and allows further leakage Obviously, great care must be taken to avoid undue pressure

Just as no anæsthetic agent is safer than the person who employs it, so no emergency ventilation method is foolproof Neonatal asphyxia is a desperate emergency and forthright methods are justified There is certainly a risk of overinflation, as Professor Pask emphasises, but it depends very largely on the diligence and care of the operator At all events, complete anoxia is a graver risk

It is unfortunately true that the securing of an airway by an accurately placed endotracheal tube may not be sufficient Positive pressure ventilation is a vital and immediate necessity in some cases of neonatal apnœa, and with the widespread use of pethidine, apnœa du to narcosis is possibly on the increase

Post mortem examinations are carried out after al neonatal deaths, and the pathologists have been particularly requested to report in detail any respiratory injury No such injury has been found On the oth hand, lungs have been described as completely atelectati when adequate inflation had been used

The intravenous needles are a more substantial safeguard than may be immediately apparent In 194 some medical officers of fighter squadrons were asked to submit reports on an oxygen economiser then in u I used a Spitfire Mk Vb kindly loaned by No 71 Squadr at Martlesham A too generous setting of the oxyge cylinder—which in those days was out of the reach o the pilot behind his armour-plating—provided me wi personal experience of overinflation I used intraven needles to provide a blow off, and know that it is a sound and practical device I gather from the accou of Lieut Commander Lithgow's recent troubles in Nort Africa that oxygen-valves still give annoyance sometim

Watford Maternity Hospital

J NOEL JACKSON

CERVICAL SPONDYLOSIS SIMULATING MOTOR-NEURONE DISEASE

SIR,—Dr Morris's letter (Oct 31) on the diagnosis of motor neurone disease seems to imply that a brisk jaw-jerk is the absolute criterion of this condition, and th a normal jaw-jerk is incompatible with a diagnosis of motor-neurone disease I am sure, however, that Dr Morris will agree that in "progressive muscular atrophy" no alteration will be found in the jaw jerk until a la stage in the development of the process, and indeed the reflex may never be abnormal Even in the "amyotrophic lateral sclerotic" form of motor neurone dis briskness of the jaw jerk may follow briskness of ot reflexes only after an appreciable interval

To complete the factual record, however, may I that in our cases of cervical spondylosis the jaw jerk not increased

The Royal Infirmary,
Manchester

L A LIVERSEDGE

RISKS OF TONSILLECTOMY

SIR,—Mr McKenzie's article last week stirs memo a quarter of a century old As house surgeon in a London children's hospital I was responsible for t twice weekly reception of 12 children, aged from 10 years, and for their care during the three days their stay Anæsthesia was by ethyl chloride (2 in a bag) *tonsillectomy* was by blunt guillotine u used as a holder whilst the forefinger of the appro hand was swept round the end of the erect guillo and invariably found the capsular plane I was ca during the night, as occasion demanded, to c hæmorrhage by pressing directly into the tonsillar with a prepared swab the size of a walnut and so in spirits of turpentine During my six months residence no vessel had to be ligatured and no died of hæmorrhage or was given a blood transfus I do not attribute this to the turpentine, but to *fact that the vessels were torn* by the dissecting finger

With regard to pain following tonsillectomy, I r the removal of the tonsils of a girl of 18 One t was held in the blunt guillotine and removed by sweep the forefinger behind the guillotine, and the other t was removed by dissection she had pain in dissected fossa and none at all on the guillotined The reason is that the pharyngeal muscles are sul to long continued and repeated damage on the dis side, whereas a blunt guillotine, slowly closed, t the capsular plane with little trauma, the finger n disrupting the various vessels which bind the t to the pharyngeal wall

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[12] Chatterjee, H N *Lancet* 1952 ii 90

How can one be sure that the blunt blade is engaging capsular cleavage? I was taught that when the de is in the right plane a concavity appears on anterior surface of the anterior pillar during the w action of closing the tip of the index finger of disengaged hand presses on the anterior pillar ite gently and keeps the tonsil posterior to the blade

ongtown Cumberland.   ROBERT RUTHERFORD

MILLI-EQUIVALENTS

SIR,—Dr Ennis's letter last week is discouraging to ose who advocate the m eq per litre terminology because its simplicity in a certain context—that of the "struc ral" electrolytes of body fluid, such as Na K Cl and CO_2 These substances are of importance chiefly in lation to one another in maintaining acid base and motic equilibrium within body fluid It is therefore gical to express their concentration in a terminology hich not only allows rapid comparison of one electrolyte ith another but also is simply related to the osmotic fect exerted by their sum. The advantages of the .eq per litre terminology have led to its general option in scientific work in this field the same merits ould commend it for general clinical use, but the draw ks mentioned by Dr Ennis certainly must be nsidered

1 The same article may express some blood constituents in .eq. per litre and others—including acid and basic radicles— a direct weight/volume terminology; this tends to con sion in understanding and in dispensing

In answer to this, no one suggests that the m eq per re terminology should be applied universally but only those electrolytes whose relationship to one another d to the osmolarity of body fluid is specially important ithin this field clarity is promoted and not lost, and it is sirable that *replacement solutions* should also be scribed in this nomenclature especially as mixed ctrolyte solutions such as Na K chloride and lactate lutions, are now being used The practical manage nt of electrolyte problems is then made easier not ore difficult

2 "The actual estimates of such substances by a laboratory *in terms of mg. per 100 ml*

This depends on the laboratory The methods of imation are in fact based on chemical equivalence or physical properties of the elements estimated and it quite as easy to use m eq per litre standards as any hers.

Most clinicians think in terms of mg per 100 ml., and w the normal blood levels so expressed.

This may be so but most people who become interested electrolyte problems or have interest forced on them responsibility find it worth while to make the small rt of self-education needed in order to reap the antage of ready comparison of different electrolyte centrations.

Our present knowledge of the part played in health disease by the electrolytes which Dr Ennis cites gests that their relationship to one another and to y water is of overriding importance rather than their ividual concentrations. The m eq per litre termin y aids this appreciation, and its application to clinical blems for it gives us our results in the units observed the electrolytes themselves in their interactions with another In the interests of our patients, we should re ourselves the struggle with incommensurate units ich is implicit in a weight/volume terminology in this ticular field.

Department of Medicine
niversity of Manchester   D A K BLACK.

SIR,—We should be grateful to Dr Ennis for wing attention to the question of marking solutions of ctrolytes for replacement therapy in m eq per litre instead of in g per litre Much of the value of using m eq per litre in reporting blood values is lost when transfusion solutions are not similarly marked The use of m.eq makes it simple to find how much of a solution is required to correct any given deficit.

Dr Ennis's argument that m eq per litre should not be used because some clinicians are accustomed to a different system, and (by implication) are unwilling to introduce any improvement, is unfair to them On such a basis we ought still to measure concentrations of replacement solutions in grains scruples, and drachms per fluid ounce, since these terms were more familiar to our ancestors than the metric ones Admittedly the retention of two systems of measurement introduces risk of error the logical action is to abandon the use of g per litre for measuring ionic substances in transfusion solutions.

Dr Ennis is wrong in stating that ionic substances are measured in the laboratory in terms of mg per 100 ml No chemist ever thinks in such terms when dealing with acids and bases the use of equivalents being much more convenient If clinical pathologists and clinicians would *make the effort, once for all, to change to similar terms* they would wonder why they ever used g per litre

Biochemistry Department,
Royal Infirmary Glasgow   J C EATON

THE INSULIN MYTH

SIR—As the one who introduced insulin therapy into this country almost twenty years ago I should like to comment on Dr Bourne's very sound article last week We must thank him for drawing attention to the fact that the "insulin-situation" makes a good deal of difference (this even holds good for E C T) and has in itself been responsible for many insulin recoveries reported Also for putting forward that prognostic and *diagnostic criteria have altered in the course of time so as* to obscure direct comparison of contemporary results with those of the pre-insulin era. I foreshadowed this[1] when remarking after a visit to Vienna that the prognosis of schizophrenia in that city at any rate appeared to be unworsening in proportion to the number of insulin recoveries reported from Poetzl's clinic alluding then to the *frigid reception that Sakel's method* was *receiving* from his local colleagues. I considered such welcome to bode well for the method's future—a view since amply confirmed by the subsequent fate of both convulsion treatment and leucotomy

I wish I could agree with Dr Bourne, though that insulin offers the schizophrenic no more benefit than does E.C.T we all should be spared a good deal of nervous energy if this were so That E C T does more for the chronic case than insulin is well known. In the more or less acute case, however, the position is reversed It is clinical experience that counts here despite all figures adduced to the contrary The uninterrupted recovery under insulin now in its twelfth year of even a single case of "hopeless" schizophrenia of two years' duration after the fruitless application of 39 E.C.T.s (by the same physician) should be enough to convince anyone that insulin is the superior treatment here[2] In particular, I have found the spontaneous insulin convulsion (which unfortunately cannot be produced at will) far more potent therapeutically than any form or number of induced convulsions, whether given on top of hypoglycæmia or otherwise

Isleworth Middlesex.   H PULLAR-STRECKER.

SIR,—Despite Dr Bourne's vigorous attack many psychiatrists will continue to use insulin-coma treatment in selected cases of schizophrenia until a *better method becomes available for they are fortified* by occasional successes. Dr Bourne will surely not deny that there are at least a few patients who remain seriously disturbed for weeks or months, despite electro-convulsion therapy and despite a good deal of attention from nurses and doctors, *until* insulin coma treatment is started If the improvement then occurs in an expected time relationship to the start of treatment, it is legitimate to conclude that the treatment *causes* the improvement

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[1] Münch med. Wschr 1936 p 649
[2] Pullar-Strecker H *Med Pr* 1944 211 319

This is the most elementary and generally applicable criterion on which to assess the value of a treatment It is surprising that Dr Bourne should have neglected it, for, although it contains a judgment of probability, it is in many respects a better criterion, when applied to each case in turn, than are the remission rates in relatively large and heterogeneous series of cases upon which Dr Bourne relies He should perhaps have taken warning from Dr Eysenck's strange experience, for a similar study of remission rates in psychoneurosis led Dr Eysenck to conclude that psychotherapy was ineffective [1]

Insulin coma treatment does relatively little damage That it has caused remission in a significant number of cases when other methods have failed justifies its use, although it has often disappointed Its immediate effects are worth while, even should it be shown—as it has not yet been—that it is ineffective in the long run

Psychological Laboratory,
Cambridge

D RUSSELL DAVIS

RECURRENT PAROTITIS

SIR,—Seven years ago I described 13 instances of this disease [2] My experience is almost identical with that noted in your annotation (Sept 26)

Rambam Government Hospital
Haifa Israel

WALTER FALK

DIAGNOSIS OF HYPERPARATHYROIDISM

SIR,—Reviewing my book, *Clinical Endocrinology*, in your issue of Oct 31, you say

> " for the diagnosis of hyperparathyroidism the aspirant will need more explicit information than is here provided surely we are not going to turn these problems over to another specialist, the chemical pathologist ? "

With regard to the first half of this sentence, an account of the disturbances of calcium and phosphorus metabolism in hyperparathyroidism has been given in detail and I should have thought could be understood by the intelligent reader, for whom the book was written The second half of your statement is truly remarkable, since hyperparathyroidism cannot be diagnosed without the services of the chemical pathologist Would you be so good as to inform us how you would arrive at the diagnosis without such assistance ?

St Bartholomew's Hospital
London E C 1

A W SPENCE

*** Dr Spence says on p 238 of his book, under the heading *diagnosis*, that " in hyperparathyroidism there is always a negative balance of calcium " This is where his aspirant might be led into error Bony changes may be absent in some severe cases of hyperparathyroidism, as Dr Spence reminds us on p 236 , this suggests that some patients maintain their stores of calcium well In fact, Dr Spence's references include an instance where the measured balance of calcium was indeed strongly positive as long as the intake of calcium was liberal The diagnosis of hyperparathyroidism may require, among other things, estimation of the urinary excretion of calcium while the intake of calcium is low , and the normal findings might also have been given But the intelligent reader can of course find, under the heading *metabolic disturbances* on p 237, that " the urinary excretion of both [calcium and phosphorus] is increased even when the intake of calcium and phosphorus is low " He mig not, however, realise that this was a condition for t test

The physician knows what radiographs to ask for an can usually interpret the findings, In the same wa when he is a clinical endocrinologist he can conduct own investigations, though he may be ignorant of chemical techniques , and he can interpret the labor results This is clearly also Dr Spence's view, since gives detailed instructions for conducting, for example the Kepler test Of course these tests cannot be without the services of a laboratory, nor indeed was suggested Some of the best work in clinical endo logy is being done by chemical pathologists, opinion, when available, is valued, but with few except they do not look after the patient —ED L

ISOLATION OF PSYCHIATRIC HOSPITALS

SIR,—In your annotation of Oct 3 (p 716) you the isolation of psychiatric hospitals and the need for association—embracing all psychiatric hospitals in country—that would provide a means for regula change of ideas

It may interest your readers that in Surrey an Inte hospital Psychiatric Association was founded just two years ago which locally fulfils this function hospitals forming the association are B Belmont, Cane Hill, Horton, Long Grove, The Netherne, St Ebba's, West Park, and the C Laboratory

The association holds regular clinical mee organised by each member hospital in rotation, at whi cases from the hospital are presented and papers read members of its staff The success of the meetings in first two years has brought forth a desire for a furt strengthening of clinical links between the hospi Recently intramural clinical conferences have thrown open to the staffs of all the member hospita the association General practitioners from the area the staff of neighbouring general hospitals attend association's meetings

We feel that there is an advantage in keeping association of this kind within the bounds of not large an area

West Park Hospital
Epsom, Surrey

JOSEPH ZELMANOWITS
Hon. secretary, Surrey Inter-hosp
Psychiatric Association.

GOUT

SIR,—As advocate of " interval " salicylate the in the treatment of gout,[1] I was naturally interested Dr Marson's paper [2] on the continuous salicylate tr ment of the disease to which your leading artic Oct 31 refers

As interval therapy now is under criticism, may I that it was suggested at a time when salicylate the took second place to the more toxic drug, cinchop because given in this way sodium salicylate cause better uric acid excretion without toxic effects It admittedly a compromise and not a complete answ the problem of the therapy of chronic gout, nor a rently is continuous salicylate therapy, which still al fluctuations in the serum uric acid level and occas attacks of acute gout, and is not always practic because of salicylism While I shall certainly try Marson's method, I was disappointed to find apparently dismissing the interval therapy on the re of only one case, thrice tested for three days out of with salicylates, which showed moderate and symp less rises in serum uric acid in the therapy inter The method has, after all, been tried and found val

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1 Eysenck H J *Quart Bull Brit psychol Soc* 1952, 3 41
2 *Harefuah* 1946 31 97

1 *Rep chron rheum Dis* 1937, 3 106
2 Marson, F G W *Quart J Med* 1953, 3, 331

experienced workers[3,4] If given for four days in ven, as I also originally suggested the upward fluc ations in the serum uric-acid level are likely to be orter and smaller, while the chances of salicylism main slight

In a longer account of my investigations on the bject,[5] I also noted the importance of a good fluid take during therapy for a patient on salicylate with high intake of bland fluid—e.g., 2400 ml daily—would ss about twice as much uric acid as during the same erapy with a low fluid intake (1200 ml) I was dis pointed to find little emphasis on the influence of fluid take on uric acid elimination during the salicylate erapy of chronic gout either in Dr Marson s paper or your leading article

Edgware General Hospital
Middlesex.

G H JENNINGS

DOSAGE OF ANÆSTHETICS

SIR,—Recent correspondence in your columns reminds that I have been using intravenous barbiturates the induction of anæsthesia for over twenty years—ree-quarters of that period in the tropics

I have observed that the temperature of the solutions the factor which appears to determine the rapidity d duration of their action

Before we had air-conditioned hospitals I noticed in e hot weather that the onset of the action of hexo rbitone (Evipan ') was more rapid than in the cold ason and in consequence less was required over a given riod.

More recently working in an air-conditioned hospital Arabia, where my patients were Americans, Arabs edouin and town dwellers) Britons Indians Iraquis alians and Red Indians I found I had to make no owance for race—merely the usual care to assess e patient s physical condition.

It would be interesting to know whether other servers have had the same experience

Northallerton
Yorkshire

J SHEOOG RUDDELL.

MEDICAL MEMBERSHIP OF HOSPITAL BOARDS

SIR,—The Institute of Public Administration held a nference in London on Oct 28–30 They discussed the alth service According to your report of the conference, John Grant said that doctors employed in a hospital ould not be appointed to the board of that hospital *This remark* your report continues *brought more plause than any other at the session* I italicise this mark lest its significance be lost. From it we can see ich way the wind is blowing The functionaries wish employ doctors in their hospitals but they do not wish em to sit at their boards to give counsel

Having reminded you of this report I feel like leaving u and your readers to chew it over without further mment, but I cannot resist a few questions Is it no nger true that patients come to hospitals to seek the vice and help of doctors ? Can you recall any major vance or reform of clinical policy within a hospital ich has been brought about without medical advice ? ve our British hospitals so bad a record over the past years that we must discard the method by which their verning bodies have received advice ?

I am all for reform where and when it is necessary but e applause of the conference of the Institute of Public ministration denotes something more than a desire r reform.

Newcastle upon Tyne

JAMES SPENCE.

Kersley G D *Brit J Rheum* 1939 2 20
Hench, P S *In* Cecil s Textbook of Medicine. Philadel, and London, 1944 p 600
M D thesis, University of Cambridge 1938 p 64

Public Health

Estimate of Future Births

THE Registrar-General s final estimate for live births in England and Wales during the December quarter is 155 000, and his provisional estimate for the March quarter 1951, is 170,000 giving an estimated total of 325 000 babies in the six months There were 158 029 live births registered in the December quarter of last year and 171 705 in the March quarter of this year—a total of 329 734 This year s number of live births registered in the 160 Great Towns up to Oct 31 was 332,083 compared with 328 062 in the same period a year ago

Sterilisation of Feeding-bottles

The Medical Research Council has completed an investigation[1] designed to assess the relative value of boiling or hypochlorite treatment for the sterilisation of infant feeding bottles and teats The laboratory experiments showed clearly that sterility of both bottles and teats could be regularly achieved either by boiling or by immersion in a hypochlorite solution, provided each method was correctly used Each method is simple but requires careful attention to detail; the complete submersion of the teat is a point often overlooked

B C G Vaccination of School children

The Minister of Health has informed local health authorities in England and Wales that he is prepared to approve schemes for giving B C G vaccination to children before they leave school; and the Department of Health for Scotland announces similar plans. Since 1949 when official permission for its use in this country was first given B C G vaccination has been offered to nurses and medical staff in hospitals and (at the discretion of chest physicians) to the close [illegible] of patients with tuberculosis. Local health [illegible] will themselves decide whether they wish [illegible] make the vaccination of school-children. Wh[illegible] be done it will be offered in coöperation with the education authority to children of thirteen [illegible] The consent of parents will always be [illegible] first. In a circular[2] setting out the details [illegible] scheme the Minister suggests that in [illegible] with the teaching staff it should be [illegible] suitable talks and discussions to eliminate [illegible] and misunderstanding that may arise among [illegible] as to the meaning of the injections and loca[illegible] reactions. The Minister has also sent to medical officers of health a memorandum discussing [illegible] of B C G vaccination

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1 *Mon Bull Minist* [illegible] 12 209 214
2 Ministry of Health [illegible]

Infectious Diseases in England and Wales

Disease	Week ended October 3	10	17	[illegible]
Diphtheria	21	[illegible]0	20	[illegible]
Dysentery	212	[illegible]07	23[illegible]	
Encephalitis				
Infective	–	3	1	
Postinfectious			1	
Food-poisoning	260	165	1[illegible]	
Measles [illegible]	622	697	[illegible]	
Meningococcal [illegible]	2[illegible]	31		
Ophthalmia [illegible]	4[illegible]	1[illegible]		
Paratyphoid [illegible]	16	1		
Pneumonia [illegible] influenzal	32[illegible]	3[illegible]		
P[illegible]				
[illegible]	7[illegible]			
[illegible]				
[illegible]	[illegible]			
[illegible]	[illegible]			
[illegible]				
[illegible]				
[illegible]				

Not including [illegible]

Notes and News

RIPENESS IS ALL

Oxford congregation has raised the retirement age of all members of the university teaching and administrative staff to 67 This is a first positive gesture towards the longer working life which we are all now invited to attempt[1] Cambridge[2] (says our Oxford correspondent) is the customary half pace behind Prof R B Braithwaite, at a meeting of the university senate on Nov 3, said that no educational advantage would be secured by following the "bad example" of Oxford, though he agreed with the Cambridge University council that wider provision should be made for using the services of retired officers He was supporting the opinion of the Master of Jesus, who maintained that not only would it be bad for the university to keep lecturers longer at their posts but also it would increase the violence of competition among younger men Mr Glyn Daniel, PH D, of St John's was one of a minority in favour of raising the retiring age to 67, the advantage of retaining brilliant teachers, he said, far outweighed the risk of prolonging the service of a few inadequate ones

Certainly, as Sir Zachary Cope pointed out at a recent conference,[3] nobody knows when a man is going to age, least of all the man himself Nevertheless the air at our great universities is known to have a peculiar preservative effect on good intellects (rather like that of the desert sands on mummies) If there is any place in the world, other than Oxford, where it should be safe to extend the working life for a couple of years, that place is surely Cambridge A compromise, however, might be wisest When a man retires at 65 the university might be given the option of inviting him to stay on from year to year, if he is willing, for as long as he seems to be contributing to the best interests of the university

ANÆSTHESIA IN CHILDREN

In his presidential address to the section of anæsthetics of the Manchester Medical Society, on Oct 29, Dr H. E Pooler discussed the administration of anæsthesia to children He described a psychiatric inquiry which had been made at Chesterfield Royal Hospital to assess the effect of tonsillectomy on a group The routine included careful preoperative preparation of the children by the anæsthetist, who explained to them why they were there and what was going to happen to them A syrup containing atropine and chloral hydrate was given by mouth before the operation Anæsthesia was induced by intravenous thiopentone followed by nitrous oxide, oxygen, and trichlorethylene The tonsils were then removed by the guillotine method. Dr Pooler suggested that the analgesic effect of trilene was carried over into the recovery period, so that the pain from the throat was subdued until the child had recovered from the effects of the thiopentone, thus minimising the postoperative restlessness commonly noted after premedication with barbiturates A psychiatric examination of 116 of these children showed that 3 4% had emotional sequelæ during the first three weeks after discharge from hospital

EDUCATION IN NUTRITION

Addressing the Food Education Society in London on Nov 4, Dr John Yudkin, professor of physiology at Queen Elizabeth College, remarked that food evoked irrational and violent emotions "There is hardly anyone who, however ignorant, however biased, is not quite certain that his own views are absolutely and completely valid, and that those who hold opposing or even somewhat different views are at the best misguided, at the worst irresponsible and malicious" Professor Yudkin touched on three common nutritional fallacies One was that purified or refined foods were necessarily inferior to the more "natural" foods if it was necessarily better to eat whole foods such as the whole wheat, because that was how it grew, why not be logical and insist on eating bananas whole too, with their skins? The second fallacy was that of "percentage composition"—that is, that the only important thing about a food was what proportion of nutrients it contained, irrespective of the amount of the food eaten. The third important fallacy was that of the panacea "I am one of those who believe it is practicable, even in our own life time, to ensure that every one of family of mankind should get the amount and the food which will satisfy his physiological needs" But th who put their faith in, and advocated, any single cours action towards this end were putting off the day when th necessary vast, multiple, and interrelated attack would made on this most urgent problem Turning to the new Lond University degree of B SC (nutrition), courses for which ha just begun at Queen Elizabeth College, Professor Yu expressed the belief that "we can produce real nutrition —not merely chemists or doctors or agriculturalists who h a leaning towards the nutritional aspects of their own specia And if we can do this, there will at last be a chance that wider education in food and nutrition—to school-chil domestic science teachers, doctors, nurses and, eventu the public as a whole—will one day be undertaken by th who have themselves studied nutrition as an integ scientific discipline and not by those who have receiv from third and fourth hand"

CONFERENCE OF ARMY PATHOLOGISTS

On the first day of this annual conference, which was in London on Oct 22 and 23, technical demonstrat arranged by the professor of pathology, were given at Royal Army Medical College, and an administrative mee was held in the War Office On the second day the follo civilian guest lecturers spoke Dr G D Lumb (Effect Radiation on the Cellular Structure of Tumours), L P Garrod (Function of the Bacteriologist in Connect with Routine Bacterial Chemotherapy), Prof A C. Fr (Gastro-intestinal Dysfunction in Man), Dr P L Mol (Hæmolytic Diseases of the Newborn), and Dr E Kath Williams (Hæmatological Control of Personnel Exposed Ionising Radiation)

FOUNDATIONS FOR A CLEARING-HOUSE

Dr N Howard Jones,[1] director of the division of edit and reference services of W H O, describes its task "documentation" as ranging from editorial selection publication (which implies ability to appraise the value of paper, with the help of expert referees) to bibliog analysis designed to make published work available to interested reader (which implies knowledge of journals, the use of indexes, bibliographies, and abstracting serv Since the work is international, the staff of the division in a team of full time translators, for though papers may the division in any known language, they are presented W H O publications in two working languages—English French

The publications of this division of W.H O include no their periodicals—the *Bulletin of the World Health Orga* the *Chronicle of the World Health Organisation*, and *International Digest of Health Legislation*—but also the *Technical Report Series* and *Monograph Series*, the *Records of the W H O*, and the supplements to the Bu Their library, now six years old, contains 30,000 volum various languages mainly on public health subjects receives 1500 current journals It gives library servi request to any of the member countries, as well as W H O headquarters' staff It seems that in this divisi may have the beginnings of that international bureau— central clearing house for scientific information—which many have foreseen as a necessity

IMPERIAL CANCER RESEARCH FUND

The Fund's new laboratories at 48, Lincoln's Inn Fie a few doors from the Royal College of Surgeons of Engl were opened on Nov 10 In 1951 the council of the F decided to support special investigations on outstan problems in the pathology of human cancer The work closely connected with the surgical treatment of canc it has been carried out for the past two years in the departm of pathology of the Royal College of Surgeons But accommodation soon proved inadequate for the gro needs of the newly recruited research staff, and the F asked the college for permission to rent its house in Linc Inn Fields and to equip it as a clinicopathological labora And the work will now have a place of its own in the splend equipped premises at no 48

The new laboratories were formally opened by Prof. H. Dean, F R.C.P, chairman of the council of the Fund, oke warmly of the help given to the venture by the Royal llege of Surgeons. The research work at Lincoln's Inn will r under the supervision of Prof Geoffrey Hadfield F.R.C.P e Fund will encourage the interchange of staff between coln's Inn and its existing laboratories at Mill Hill which main under the direction of Dr James Craigie F.R.S

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[1] *Lancet* Oct. 24, 1953, p 871
[2] *Times* Nov 4 1953
[3] Second Health Services Conference, Oct. 28–30 1953

[1] *Bull. med Libr Ass* 1953, 41, 101

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iversity of Oxford

On Oct 31 the following degrees were conferred:

D.M.—E. O Field, Ebbe C. Hoff R. G White

iversity of Cambridge

On Oct 31 the following degrees were conferred:

M.A—C. W McE Pratt.
M.D.—T M. Robinson, R. B Welbourn D H M Woollam
M.B., B.Chir—Stella M L. Ambache

iversity of Edinburgh

On Nov 4 the Duke of Edinburgh the newly installed ncellor conferred the honorary degree of LL.D on Sir xander Fleming F.R.S

yal College of Physicians of Edinburgh

At a meeting on Nov 3 with Dr W A Alexander the sident, in the chair the following were elected to the owship

L V Rajam, Sir Peter MacCallum Robert Morrison, Jean M unt, G H Armitage, Sujata Chaudhuri, I R. C Batchelor G S Hill, E M Heller R C. L. Batchelor J O Forfar A. Karunaratne, J H Wright, G M Fyfe

The following were elected to the membership:

C K. Maclachlan, E Hacker S S Maitra, L. D Walters D A idlow E Taube V M. Herous, W. Cooper R L. Walker H ason, J O Taubman, M G Pradhan, F W Tadros, J D drew S. A. Biggart, G R. Tudhope, D W Dawson H M cleod, N K. Sarkar S Sachdev J D Haldane A K. Dutta P Kumbhani T T S Ingram, B Zilberg J Blake.

yal Faculty of Physicians and Surgeons of Glasgow

The following have been elected office bearers for the ning year

resident, Dr Andrew Allison, visitor Prof. Stanley G Graham n. secretary Dr A. H Imrie hon. treasurer Mr Matthew ite; hon. librarian, Dr Archibald L Goodall; representative the General Medical Council, Dr Andrew Allison councillors f. D F Cappell Prof. Leslie J Davis, Mr Walter W Galbraith mediate past president), Dr A. D Telford Govan, Prof. C. F W nworth, Dr Samuel Lazarus Dr J A W McCluskie, Mr Ferguson Mackenzie Prof. W Arthur Mackey Dr Thomas ople and Dr Gavin B Shaw

Mr J J Mason Brown will deliver the Dr John Burns ture in the hall of the faculty 242 St Vincent Street on dnesday Nov 18 at 5 P.M. He is to speak on the Surgical atment of Anomalies of the Alimentary Tract in the wborn.

sociation of Surgeons of Great Britain and Ireland

Next year the association's annual meeting is to be held Leeds on May 13 14 and 15 The subjects to be discussed lude hiatus hernia ulcerative colitis exophthalmos and odenal diverticula

berden Society

Sir Russell Brain F.R.C.P will deliver the Heberden ation on Friday Dec 4 at 3 30 P.M at the Royal College Surgeons, Lincoln's Inn Fields, W C 2 He is to speak on ondylosis: The Known and the Unknown

itish Council for Rehabilitation

On Wednesday Nov 25 the council is holding a one-day ference in association with the department of social dicine of the University of Sheffield at the university medi library starting at 10 A.M The subject will be Can abilities be Overcome?

ited Hospitals Festival Choir

This choir conducted by Colin Ratcliffe is to give two certs at the Royal Albert Hall during 1954 The first, art's *Requiem*, with the Philharmonia Orchestra, will be Jan. 20 and the second probably Verdi's *Requiem*, with London Symphony Orchestra, during the summer hearsals are held every Thursday between 6 P.M and P.M at the Church of the Most Holy Trinity Brompton mbership is open to anyone who works in a hospital, and plications will also be considered from anyone who has done in the past There are vacancies for all voices. Further rticulars may be had from the secretary Flat I 93 Lexham rdens W 8

Royal Society

The Copley medal has been awarded to Prof A J Kluyver FOR MEM R.S., for his contributions to the science of microbiology

Royal Institute of Public Health and Hygiene

Sir Henry Dale O.M F.R.S is to deliver the Harben lectures at the institute 28 Portland Place London W 1, at 5 P.M on Monday Tuesday and Wednesday Dec 7 8 and 9 His subject will be Changes and Prospects in Medicinal Treatment

Alfred Adler Medical Society

At a meeting to be held at 11 Chandos Street London, W 1 on Thursday Nov 12 at 8 P.M Dr T F Cotton will speak on the Psychological Element in Cardiac Disease

Robert Roesler de Villiers Award

On Oct 20 this award was conferred on Dr Ludwik Gross chief of research at the Veterans Administration Hospital Bronx New York, for his work on leukæmia.

Society of Public Analysts

At the next meeting of the society to be held on Wednesday Dec 2 at Burlington House London W 1 at 7 P.M Prof C H Gray will give a lecture on Recent Advances in Medical Chemistry

World Congress of Catholic Doctors

The main subject chosen for discussion at this congress, which is to be held in Dublin from June 30 to July 4 is Demography Further particulars may be had from the secretariat of the congress at Veritas House 7 Lower Abbey Street Dublin

London Jewish Hospital Medical Society

At a meeting of this society to be held at 8 30 P.M on Thursday Nov 20 at 11 Chandos Street, W 1 Sir John Parkinson will speak on Syncope

International Gerontology Congress

The 3rd Congress of the International Association of Gerontology is to be held in London on July 10–23 1954 The chairman of the British organising committee is Prof R E Tunbridge and the British organising secretary is Mrs. A Humpage Tavistock House South Tavistock Square London W C 1

Society for Cultural Relations with U S.S R

Dr Ilina chairman of the executive council of the Medical Workers Union in the U.S.S R., and Dr Kazantseva director of the Institute of Pædiatrics of the Soviet Academy of Medical Sciences, are visiting this country; and this society has arranged for them to address a meeting intended for doctors, on Monday Nov 30 at 8 P.M at the house of the society 14 Kensington Square London W 8 They are to speak on pædiatrics in the U.S S R

Provision for Old Age

The committee which, under the chairmanship of Sir Thomas Phillips, is reviewing the economic and financial problems arising from the changing age-structure of the population (but not with specific levels of provision for the individual pensioner) would welcome evidence from individuals, institutions, and organisations. Evidence in the form of written memoranda should be submitted to the joint secretaries of the committee Treasury Chambers, Great George Street London S W 1 not later than March 31

British Cardiac Society

The autumn meeting of this society was held in London on Oct. 30 under the chairmanship of Sir John Parkinson Short communications arranged by Dr Samuel Oram the secretary included papers on sodium chloride and cardiac muscle; pulmonary distensibility and respiratory work in mitral stenosis; cardiac output during exercise measured by the Fick method; pulmonary venous drainage into the right heart via a persistent left superior vena cava entering the left innominate vein; and the ballistogram in coronary artery disease

Diary of the Week

NOV 15 TO 21

Monday, 16th

Postgraduate Medical School of London, Ducane Road W 12
4 P.M Prof F J Nattrass Difficulty in Diagnosis of Epilepsy

Royal Eye Hospital, St George's Circus, S E 1
5 30 P M Miss J M Dollar Ophthalmic Nursing and Post operative Treatment.

Institute of Cardiology, National Heart Hospital Westmoreland Street, W 1
9 30 A.M Sir John Parkinson Pain in the Chest

Hunterian Society
8 30 P M (Apothecaries' Hall, Black Friars Lane E C 4) Proposers Mr A Dickson Wright Dr R. R. Bomford Opposers Sir Malcolm Hilbery, Q C, Dr H Joules That Tobacco is a Blessing

Tuesday, 17th

British Postgraduate Medical Federation
5 30 P M (London School of Hygiene and Tropical Medicine, Keppel Street, W C 1) Prof W T Astbury F R.S *Proteins and other Biological Macromolecules*

Society of Apothecaries of London, Black Friars Lane, Queen Victoria Street E C 4
4 P M *Dr Peter Bishop Disorders of Sex*
5 15 P.M Dr W S C Copeman Chronic Rheumatic Diseases—*a Revaluation of Remedies*

Institute of Dermatology, St John's Hospital Lisle Street, W C 2
5 30 P.M Dr E J Moynahan Connective Tissue

West End Hospital for Nervous Diseases, 40 Marylebone Lane, W 1
5 30 P M Dr D Gordon Neuroradiological demonstration

Manchester Medical Society
4 30 P M (Medical School, University of Manchester) Sir Zachary Cope Birth of Modern Medicine

Wednesday, 18th

Postgraduate Medical School of London
2 P M Prof F G Young, F.R.S Endocrine Control of Carbohydrate Metabolism (First of two lectures)

Royal Society of Medicine 1, Wimpole Street W 1
8 15 P M *Section of General Practice* Dr John Fry Prof J G Scadding Dr Peter Kerley Common Lung Infections in General Practice

Royal Eye Hospital
5 30 P.M Mr J F P Deller Optics of Direct and Indirect Ophthalmoscopy

Royal Institute of Public Health and Hygiene, 28, Portland Place W 1
3 30 P.M Dr G B Mitchell Heggs *Dermatology in Industry*

Institute of Dermatology
5 30 P M Dr J O Oliver Bacteriology of Skin Diseases

Institute of Urology 10, Henrietta Street, W C 2
5 P M Mr D I Williams Retention of Urine in Childhood

Eugenics Society
5 30 P M (Burlington House, Piccadilly, W 1) Mr G Aird Whyte, Dr C P Blacker Possible Future Activities of the Eugenics Society

Thursday, 19th

Royal College of Physicians Pall Mall East, S W 1
5 P M Mr B Ifor Evans D LIT Science and Literature (Lloyd Roberts lecture)

Royal College of Surgeons, Lincoln's Inn Fields W C 2
3 45 P M Dr B E Heard Sites of Common Malignant Tumours (Erasmus Wilson demonstration.)

College of General Practitioners
5 45 P M (Society of Apothecaries, 14 Black Friars Lane, E C 4) Dr Stephen Hadfield Medical Ethics and the *Pitfalls of General Practice*

British Postgraduate Medical Federation
5 30 P.M. (London School of Hygiene and Tropical Medicine) Prof G W Harris F R S Stress and Thyroid Activity

Postgraduate Medical School of London
11 A.M. Professor Young Endocrine Control of Carbohydrate Metabolism (Second of two lectures)

Royal Army Medical College Millbank S W 1
5 P M Sir Stanford Cade Modern Conception of Treatment of Cancer

Royal Statistical Society
6 P.M (2, Savoy Hill W C 2) Dr Richard Doll Smoking and Cancer of Lung (Joint meeting with Study Circle on Medical Statistics)

British Institute of Radiology, 32 Welbeck Street, W 1
8 P M Dr Sheila Callender Dr John Badenoch Use of Radioactive Iron in Investigation of Anæmia Mr E H Belcher, PH D Mr I G F Gilbert, Mr L F Lamerton M.SC Experimental Studies with Radioactive Iron

Institute of Laryngology and Otology, 330, Gray's Inn Road, W C 1
5 P.M Prof F C Ormerod Malignant Disease of the Bronchus

Research Defence Society
5 30 P.M (University College Gower Street W C 1) Sir James Learmonth, The Surgeon's Debt to Animal Experiment

Charterhouse Rheumatic Clinic, 56, Weymouth Street, W.1
5 P M Dr J F Brailsford Prevention Detection and Treatment of Osteo arthritis (Gilbert Scott lecture)

Honyman Gillespie Lecture
5 P M (University New Buildings, Teviot Place Edinburgh) Prof A C P Campbell Weil's Disease

Friday, 20th

Postgraduate Medical School of London
4 P M Dr C S Hallpike Vestibular Disorders.

Royal Society of Medicine
4 30 P M. *Section of Epidemiology* Prof T Francis, jun. (A Arbor, Michigan), Prof C H Stuart Harris Serological and Epidemiological Observations on
8 15 P.M *Section of Radiology* Dr J Boland, Dr R. C. T Prof R. McWhirter Trends in Radiotherapy at Seventh International Congress of Radiology

Faculty of Radiologists
4 15 P M (Royal College of Surgeons) Dr Walter Dr C L Lewis, Dr Frank Ellis Carcinoma of Ovary

Institute of Dermatology
5 30 P.M Dr Moynahan Scleroderma and Allied Conditions

Institute of Laryngology and Otology
4 30 P.M Prof Victor Lambert Changing Pattern of C and Laryngology

University of Cambridge
4 30 P M (Department of Pathology, Tennis Court Dr Sven Moeschlin (Zürich) Immunological A Agranulocytosis

Appointments

Aitken, J C, M.B Glasg, D P.H asst M O for Norfolk C Council, and M O H for Depwade rural, London rural urban and Wymondham urban districts

Harkness, John, M.D, B.SC Glasg area pathologist, S Somerset clinical area

Holtby, G R M D Lond asst M O for Norfolk County C and M O H for Blofield and Flegg rural Smallburgh and North Walsham urban districts

More Eleanor, M B Edin D P H school M O., Notti educational committee

Prettejohn, E J T, M B Camb, M R C P consultant der logist, South Somerset clinical area.

Scadding F H M D Lond, M R C P asst physician (consult Middlesex Hospital London

Appointed Factory Doctors

Innes C R M B Aberd for Barra, Inverness-shire

Jeffrey J C S, M B E, M B Aberd for Nesting (No. distr Shetland

Owen, J W M, M.R.C S for Plympton Devon

Manchester Regional Hospital Board

Blair J D, M B Glasg, D A consultant anæsthetist, Lan and Kendal hospitals

Buchan, A P, M B Aberd., D P H deputy medical supe tendent, and asst. psychiatrist, Brockhall Hospital, L near Blackburn

Gibb Robert, M B Aberd, F F R, D M.R E consultant therapist, Christie Hospital, Manchester

Parry, H E, M B Lond, M R C P, D C.H deputy phys superintendent, Monsall Hospital, Manchester

Pollock, Margery, M.B Dubl, D.A consultant anæ Royal Manchester Children's Hospital, and Salford Hospital.

Rains Kathleen, M R C S D A consultant anæ North Manchester hospitals, and Booth Hall Ch Hospital Manchester

Newcastle Regional Hospital Board

Fastham, R. D, B A, M D Camb D C.P DIP.PATH co pathologist Newcastle General Hospital

Fitzpatrick G A M D, B.SC. Glasg, D P.M medical s tendent and consultant psychiatrist Cherry Know pital Ryhope near Sunderland

Gibson J B, M B Glasg, D A consultant anæ Wansbeck and Alnwick, H.M C.S

North East Metropolitan Regional Hospital Board

Dixon, J H, M.A, M B Camb D A part time anæ (consultant) Black Notley and Broomfield Hospitals

Hans, S F, M D Lond F R C.S M.R C O G part-time o rician and gynæcologist (consultant) Epping group hospitals

Klein Miklos, M D Pécs D O.M S part time ophth surgeon (consultant) London Jewish Hospital

Mayer Helen M R C O G part time gynæcologist (consu Mildmay Mission Hospital

Zuck David, M.B Birm, F F A, D.A full time anæs (consultant), Chase Farm Hospital and group

Births, Marriages, and Deaths

BIRTHS

Copland.—On Nov 1 at Southmead Hospital, Brist Dr Elizabeth Jane Copland (née Hunter) wife of Dr W Copland—a daughter (Rosalind Susan)

CORONARY HEART-DISEASE AND PHYSICAL ACTIVITY OF WORK

J N MORRIS
Glasg., M.R C.P., D P.H.

J A HEADY
M.A. Oxfd

HE SOCIAL MEDICINE RESEARCH UNIT MEDICAL RESEARCH COUNCIL

P A B RAFFLE
M.D Lond. D P.H D I H.

HE MEDICAL DEPARTMENT LONDON TRANSPORT EXECUTIVE

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his report is one of a series on the epidemiology of nary disease Study of coronary heart-disease[10] ests that there has been a true increase of it, and this is not due simply to an increase of coronary roma. The atheroma it seems, is the basic condition e heart-disease but other conditions are necessary the complex of atheroma, thrombosis, and the city of the heart to deal with these in relation to the ands made upon it, all need to be studied

rveys have been made from the Social Medicine earch Unit to gain some knowledge of coronary heart-ase as a problem in public health and in the hope ncovering social factors which may be favourable or vourable to its occurrence Observations on a group edical practitioners[12] indicated that such epidemio al study can be carried out with relatively small bers, and that it may be rewarding The present rt extends this study to other workers and describes findings among them Readers are referred to the ious papers where the possibilities and limitations his type of investigation are considered, and points heory and method are discussed in some detail

CORONARY HEART DISEASE IN DIFFERENT OCCUPATIONS

London Transport

he occurrence of coronary heart-disease in certain ps of weekly paid employees of London Transport cutive during 1949 and 1950 was studied by special ngement between the unit and the Chief Medical er and Staff Administration Officer of London sport Executive The experience of drivers and uctors of the Central (red) buses, the drivers and uctors of the trams and trolleybuses, and the motor and guards on the Underground railways was rved. About 31 000 men aged 35 to 64 were lded. These groups of staff were chosen because the bers in each grade were large and the groups were ogeneous as regards occupation

investigations of this type two sets of facts are red

Facts about all the episodes of coronary heart-disease were recognised during the period under review and t the workers concerned

) Facts about the populations to which these workers ged.

his information was obtained in the manner described w

Part of the general study of industrial morbidity being by the London Transport Executive[13] all sickness nces of any duration for these 31 000 employees are ded in a Central Record of Staff Statistics maintained by Staff Administration Officer Medical diagnoses are ned from general practitioners and hospital certificates, from the London Transport medical officers who examine before they return to work if their absence exceeds ty-eight days. In addition cases of heart-disease with absences of any duration are so examined. All diagnoses are coded by the International three figure code.[9] Details of all deaths and of all retirements due to ill health are also recorded and the medical causes are similarly coded Copies of the death certificates were available, as were the diagnoses of the London Transport medical officers for ill health retirements. Routine checks are imposed in the Central Record of Staff Statistics to ensure accuracy of data

By special arrangement for the present inquiry all absences, ill health retirements, and deaths, the diagnoses of which were assigned to any code number from 420 to 434 (inclusive) were reported to the medical department for detailed scrutiny and cases of coronary heart-disease, presumptively atherosclerotic, and doubtful cases for consideration were then notified to the unit. (It is of course to be appreciated that all clinical presentations of the disease whether occurring on or off duty were included.)

From the Central Record of Staff Statistics population counts in appropriate age-groups for each occupational group were available at the beginning and end of each year the investigation covered

RESULTS

Incidence and Early Mortality

Men may retire from work because of coronary heart-disease so information from industrial sources on

TABLE I—FIRST CLINICAL EPISODES (INCIDENCE) OF CORONARY HEART DISEASE IN WEEKLY PAID STAFF (MEN AGED 35–64 INCLUSIVE) OF LONDON TRANSPORT EXECUTIVE, 1949–50

Ages (years)	(1) Angina pectoris		Coronary thrombosis				Total incidence	
			(2) Coronary occlusion—myocardial infarction		(3) Immediate mortality			
	No. of cases	*Rate per 1000 p.a.*	No. of cases	*Rate per 1000 p.a.*	No. of cases	*Rate per 1000 p.a.*	No. of cases	*Rate per 1000 p.a.*
35–39	0		2		0		2	
40–44	1		3	*0·3*	2		6	*0·6*
45–49	1		12	*1·1*	6	*0·8*	19	*1·8*
50–54	3	*0·3*	14	*1·5*	9	*1·0*	26	*2·9*
55–59	11	*1·6*	13	*1·9*	8	*1·2*	32	*4·6*
60–64	6	*1·2*	19	*3·8*	9	*1·8*	34	*6·9*
Total no of cases	22		63		34		119	
Standardised rate at ages 35–64 incl		*0·4*		*1·2*		*0·7*		*2·3*

First clinical episode = clinical onset of disease = the first recognised and recorded attack of coronary (ischæmic) heart-disease. This was taken to be the same as the first absence from work ascribed to coronary heart-disease All sickness absences of any duration were recorded and all deaths are known. The experience of the men during 1949–50 was observed concurrently and related to their personal records with London Transport Executive and predecessor organisations. Only episodes which began in 1949 and 1950 were included

The type of first clinical presentation is taken from the final diagnosis for the first absence from work with London Transport Executive which was ascribed to coronary heart-disease. There were three main types (1) angina pectoris or of effort causing sickness absence for more than 3 days (2) "coronary thrombosis" —coronary occlusion—myocardial (cardiac) infarction causing sickness absence for more than 3 days (3) Immediate mortality in which are included sudden deaths from coronary heart-disease deaths occurring on duty or during the first 3 days of the first recorded absence from work for coronary disease Cases of "coronary insufficiency" &c., are included with "coronary thrombosis" in (2).

Rate of first clinical episode—Rates in this report are usually average annual rates per 1000 The rate of first clinical episode, or attack, may be termed the "incidence" Since the incidence of individual types will be considered the total rate is better described as the total incidence and is the sum of the rates of (1) (2), and (3) above

The *rates* are standardised for age to permit comparison of the experience of the various groups of workers. The base is the male civilian population of England and Wales in mid 1949

Throughout these tables the numbers of cases are in roman type *rates are in italics* No *rates* are calculated for less than 3 cases.

X

episodes of it later than the *first* is liable to be incomplete We are therefore dealing at present only with the *first absence from work* because of coronary heart-disease, this first absence being regarded as the first clinical episode Table I and fig 1 set out the "incidence"—that is the rate of occurrence of first clinical episodes in the men who were studied The disease is uncommon till 45 years of age, as the last columns of the table show, and from then the incidence rises steadily to 6 9 per 1000 per year at 60–64 years of age

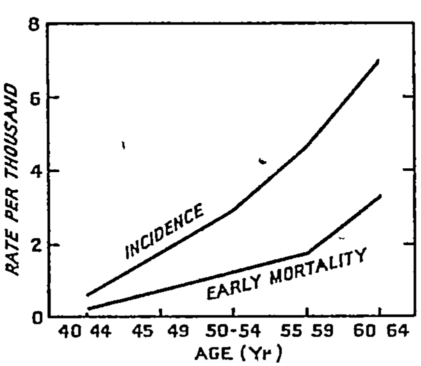

Fig 1—First clinical episodes (incidence) of coronary heart-disease, together with mortality in the first three months, in weekly paid male staff of London Transport Executive in 1949-50

There were three main ways in which the disease first presented itself clinically

1 As *angina pectoris,* representing almost one fifth of all the cases

2 As an attack of "*coronary thrombosis*"—coronary occlusion—myocardial (cardiac) infarction that was not rapidly fatal about one half

3 As "coronary thrombosis" causing death in the first three days of the first clinical episode (here called "*immediate mortality*") between a quarter and a third of the total

Angina of effort, as expected, is rarely diagnosed under 50 years of age, on the other hand, there is no particular tendency for the rapidly fatal cases to occur at younger ages The highest incidence of angina is in men in their late 50s

Fig 1 sets out also the deaths from coronary heart-disease that occurred among these men during the first three months of their clinical disease This "early mortality," as it will be called, rises to 3 2 per 1000 per year at 60–64 years of age Far more deaths occurred "immediately," in the first three days of the clinical disease (34 deaths, table I), than in the rest of the first three months (a further 15 deaths), a finding that agrees with that of the medical practitioners previously studied [12] The standardised rates are 0 7 for "immediate mortality" and 1 0 for the total "early mortality" (49 deaths)

Early Prognosis

Table I shows that over a quarter of all diagnosed cases were fatal in the first three days (34 of 119), this "case-fatality" is fairly stable in each age group In all, about 40% of the first clinical episodes of the were fatal during the first three months (49 of The size of this proportion may surprise those experience is limited to hospital medicine, but it be realised that many of these cases would not be in hospitals unless they were B(rought) I(n) D(ead).

The early prognosis, of course, varies with the manner in which the disease first itself, angina pectoris being the most benign form the point of view of fatality Only 1 of the 22 men presenting with angina died in the first three of the clinical disease, compared with 48 of the (63 + 34, table I) who presented as cases of " thrombosis"—myocardial infarction The ad of those who first present with angina of effort is clear for the three months observed. Other ev shows that this advantage continues for some least It seems that when coronary heart-disease presents clinically as angina of effort the prognosis same as in men who have survived the dangerous weeks of a first attack of "coronary thrombosis myocardial infarction

THE EXPERIENCE OF DRIVERS AND CONDUCTO

Our main object was to seek for relations betwee kind of work men do (understood throughout this in the sense of paid employment) and the incidence them of coronary heart-disease The inquiry therefore designed to show up differences in the of different occupational groups Two years' data obtained for the workers on central buses, trams trolleybuses, and preliminary examination of the (table II) suggested that coronary heart-disease be differently in the drivers and in the conductors brief, angina pectoris was relatively commoner among conductors, rapidly fatal "coronary thrombosis" the drivers 13% of the first episodes among the d took the form of angina—or were so diagno compared with 39% in the conductors Contrari the "immediate" deaths accounted for 31% drivers (25 "immediate" deaths in 80 cases) as 19% in the conductors

In table III the *annual rates of incidence* are cal for ten year age brackets, and *standardised rates* (the population structure of England and Wales basis) are also presented the more readily to comparison between groups of different age compo It will be seen that the total incidence is higher drivers (2 7 compared with 1 9) and there is a sugg that the disease appears at a younger age in More remarkable, the immediate mortality is over as high in the drivers On the other hand, the in of angina is twice as great in the conductors (0·8 per against 0 4) These trends form a pattern wh seen at each ten-year age group, the sole exc being that the one man with angina under 45

TABLE II—TYPE OF FIRST CLINICAL PRESENTATION OF CORONARY HEART-DISEASE IN DIFFERENT OCCUPATIONS AGED 35–64 INCLUSIVE) OF LONDON TRANSPORT EXECUTIVE, 1949–50

Numbers of Cases in the Different Occupations

First clinical presentation	Drivers			Conductors			Motormen and guards, railways†
	Central buses	Trams and trolleybuses	(%)	Central buses	Trams and trolleybuses	(%)	
Angina pectoris	9	1	13*	10	2	39*	0
Coronary thrombosis"—myocardial infarction &c surviving 3 days	35	10	56	10	3	42	5
Immediate mortality (first 3 days)	20	5	31	6	0	19	3
Total no of cases Man years observed	64 21 464	16 9262	100 30 726	26 12,971	5 6195	100 19 166	8 5902

Definitions &c as in table I

*Percentage of angina among all the cases added together, in each of the two groups—drivers and conductors—and similarly for the types of clinical presentation. These workers are in social class III, except for conductors who are in IV

only for 1950

BLE III—FIRST CLINICAL EPISODES OF CORONARY HEART DISEASE IN DRIVERS AND MALE CONDUCTORS (AGED 35–64 NCLUSIVE) OF CENTRAL BUSES TRAMS AND TROLLEYBUSES F LONDON TRANSPORT EXECUTIVE, 1949–50

Average Annual Rates per 1000

ges (years)	Man years observed	Angina pectoris	"Coronary thrombosis"		Total incidence	
			Coronary occlusion—myocardial infarction	Immediate mortality (first 3 days)	No of cases	*Rate per 1000 p.a*
Drivers						
–44	12 360		*0 4*		8	*0 7*
–54	11 698	–	*1 5*	*0 9*	29	*2 5*
–64	6668	*1 2*	*3 3*	*2 0*	43	*6 5*
ndardised rate at ages 35–64 incl.		*0 4*	*1 5*	*0 9*		*2 7*
Conductors						
–44	962*				0	
–54	5522	*0 3*	*0 9*	*0 5*	11	*2 0*
–64	4022	*2 2*	*2 0*	*0 8*	20	*5 0*
ndardised rate at ages 35–64 incl.		*0 8*	*0 8*	*0 4*		*1 9*

Definitions as in table I.
Cases as in table II

* †† $0{\cdot}001 < P < 0{\cdot}01$ (testing the difference between the drivers and conductors in the distribution of the number of cases among the three types of presentation).

ver (As a matter of fact with this exception the tern was found in each of the six five year groups in 35–64) The present type of inquiry is not suitable considering the niceties of morbidity diagnosis. should however be noted that the diagnosis of ngina pectoris is likely to be a self-correcting one, l if rest pain appeared during the first recognised ess from coronary disease the diagnosis stood a d chance of being amended at one of the several tinies of each case that took place during the inquiry a routine measure the final and most serious diagnosis any episode was used in drawing up the tables, and re was ample opportunity to change the diagnosis he light of experience

able IV redistributes the data Column 3 is the total dence again Column 2 gives the mortality during first three months, and it shows that the higher tality among the drivers in the first three days of disease already noticed in table *III* (*0 9 compared* h 0·4) continues for the rest of the first three months, total early mortality rates being 1 3 and 0 6 The y case-fatality among the drivers is almost 50% of 80) compared with 30% in the conductors (9 of leaving the rate of survivors, column 1 the same in h groups.

oncluding then and from the more interesting point iew the conductors had less coronary heart-disease n the drivers, and the disease seemed to be appearing them at a later age What disease the conductors was less severe: they had a smaller early case lity as well as a lower incidence and therefore they a substantially lower early mortality rate On other hand, the conductors had so much of their more ign type of disease in the form (or diagnosis) of ina pectoris that they had absolutely as well as tively a higher incidence of angina than the drivers

DISCUSSION

Four questions arise Is this kind of analysis worth ing at all? Is it likely that the differences which emerge mean anything? Do they suggest any answers likely to be relevant to the ætiology of coronary heart disease? And do they indicate any further questions?

Reliability of Observations

The method of investigation involved primarily two sets of physicians—the men's own general practitioners, and the medical officers of London Transport Executive In addition, there is documented "confirmation" by a specialist, or a hospital or in a few cases only, by an electrocardiogram in over 90% of the non fatal cases this suggests that there was a reasonable standard of diagnosis Because of the methods of collection of data in London Transport all diagnosed cases are likely to be included The main point however is that this is an epidemiological study of the experience of different occupational *groups* There is no reason whatever to suppose that the standard of diagnosis, whether good or merely adequate, or the completeness of ascertainment, will differ in the groups being studied The population consists of men from the same part of the country, served by the same health and welfare services and living in broadly similar social circumstances during the same period of time Conditions of sickness absence and sickness benefit are similar throughout It seems reasonable and worth while therefore to compare the experience of various groups within London Transport

Their Significance"

The main finding is that the conductors have a pattern of incidence of coronary heart disease different from that of the drivers Is this a chance phenomenon? Statistical tests suggest that it is unlikely It is also worth recollecting that although numbers of cases are too small for many rates to be calculated, the distribution of the various types of first presentation of coronary heart disease differs in the conductors of *central buses* from that of the drivers of central buses (table II) likewise the distribution of cases in the *tram and trolleybus* conductors differs

TABLE IV—EARLY OUTCOME OF FIRST CLINICAL EPISODES OF CORONARY HEART DISEASE IN DRIVERS AND MALE CONDUCTORS (AGED 35–64 INCLUSIVE) OF CENTRAL BUSES, TRAMS AND TROLLEYBUSES OF LONDON TRANSPORT EXECUTIVE, 1949–50

Average Annual Rates per 1000

Ages (years)	(1) Rate surviving first 3 months	(2) Rate dying in first 3 months	(3) Total incidence
Drivers			
35–44	*0 4*	*0 2*	*0 7*
45–54	*1 4*	*1 1*	*2 5*
55–64	*3 2*	*3 3*	*6 5*
Total no of cases	42	38	80
Standardised rate at ages 35–64 incl.	*1 4*	*1 3*	*2 7*
Conductors			
35–44			
45–54	*1 3*	*0 7*	*2·0*
55–64	*3 7*	*1 3*	*5 0*
Total no of cases	22	9	31
Standardised rate at ages 35–64 incl	*1 4*	*0 6*	*1 9*

(1) Surviving first 3 months includes all men in whatever way coronary heart-disease first presented in them (as angina of effort or as "coronary thrombosis"—myocardial infarction), who were alive on the 90th day after the onset of the first clinical episode of the disease

(2) "Dying in first 3 months" = early mortality

$0{\cdot}001 < P < 0{\cdot}01$ comparing the totals of cols. (2) using the t test.

TABLE V—FIRST CLINICAL EPISODES (INCIDENCE) OF CORONARY HEART DISEASE IN MALE POSTAL WORKERS AND CIVIL SERVANTS (AGED 35–59 INCLUSIVE), 1949–50

Average Annual Rates per 1000

Ages (years)	Rate surviving first 3 months		Rate dying in first 3 months	Total incidence	
	Angina pectoris	"Coronary thrombosis"—myocardial infarction	Coronary heart-disease	No of cases	*Rate per 1000 p a*
35–39	*0 1*	*0 1*	*0 2*	13	*0 4*
40–44	*0 1*	*0 2*	*0 5*	24	*0 8*
45–49	*0 6*	*0 5*	*0 8*	60	*1 9*
50–54	*0 9*	*1 3*	*1 3*	187	*3 6*
55–59	*1 2*	*1 7*	*2 0*	153	*4 9*
Total no of cases	113	144	180	437	
Standardised rate at ages 35–59 incl	*0 5*	*0 6*	*0 9*		*2 0*

Definitions as in tables I and IV

The postal workers were observed for 1949–50 the Civil Servants (executes and clerks) for 1949 Only established men were included

The "populations" were calculated from special counts as on April 1, 1949, and April 1, 1950

from that in their drivers, moreover, the experience of the two groups of conductors is similar, as is that of the two groups of drivers

Their Interest

What we are looking for, mainly, are useful hypotheses on the causes of coronary heart disease The present observations suggest that in the experience of these conductors and drivers there are real differences which are not due to faulty data or small numbers Here then is a "way in" to the exploration of possible causes Three explanations that might lie behind the differences in incidence and mortality at once come to mind

1 That they are due to differences in the *constitution* and early experience of the conductors and drivers, another expression of which is that the men select for themselves these very different jobs

2 That while there may be *mental strains* in both driving and conducting, these may be of different kinds and the difference may be a factor in the higher incidence and mortality among the drivers

3 That the greater *physical activity* of "conducting" (on these double decker vehicles) is a cause of the lower incidence and mortality in the conductors

It is easy to imagine *all* of these influences contributing to the difference of experience observed (and there may be many more) It is interesting, however, that, so far as the one year's experience goes, the Underground railwaymen (table II) had a pattern of disease similar to that of the road-vehicle drivers The most obvious way in which these railway workers resemble the drivers and differ from the conductors is in the degree of physical activity involved on the job This last proposition—that the physical effort in the conductors' work may be a protective factor, safeguarding them in middle age from some of the worst manifestations of coronary heart disease suffered by less active workers—attracts us most, because it offers special opportunities for study We therefore decided to focus on it for a start, and to ignore the other factors in the constitution of the men and in their history that must certainly also be involved We were further persuaded to do so by a parallel investigation which was made in the Post Office and Civil Service, the results of which became available soon after those of the transport workers

Postal Workers and Civil Servants

During 1949–50 the Treasury Medical Service also ascertaining cases of coronary heart-disease reporting them to the unit Their procedure was follows

Men aged 35–59 years in particular were studied (b of the frequent retirement after 60) and the inquiry limited to "established" personnel, the "population" which was specially enumerated from the Central Staff P by the Organisation and Methods Division of the T Male postal workers in the following grades were incl

Postmen.
Postmen higher grade
Postal and telegraph officers
Supervisors
Telephonists

In addition, established men in the executive and grades of most of the Ministries served by the T Medical Service (i e, most of what is usually termed t Service) were observed The postal workers are in the trar General's social class III, the executive officers in and the clerical grades in both II and III

All sickness absences ascribed to coronary heart- related conditions, or to conditions which were

TABLE VI—FIRST CLINICAL EPISODES OF CORONARY DISEASE IN MALE POSTAL WORKERS AND CIVIL (AGED 35–59 INCLUSIVE), 1949–50 INCIDENCE WITH PHYSICAL ACTIVITY

Average Annual Rates per 1000

Ages (years)	Man years observed	(1) Rate surviving first 3 months		(2) Rate dying in first 3 months	(3) Total
		Angina pectoris	"Coronary thrombosis"—myocardial infarction	Coronary heart disease	No of cases
A Postmen 35–44	29 145	*0 2*	*0 1*	*0 1*	13
45–54	35,782	*1 1*	*0 8*	*0 8*	90
55–59	13,577	*1 2*	*1 6*	*1 8*	67
Total no of cases		61	53	57	171
Standardised rate at ages 35–59 incl		*0 7*	*0 6*	*0 6*	
B Intermediate grades 35–44	20,052			*0 5*	[illegible]
45–54	24 397	*0 6*	*1 1*	*1 1*	69
55–59	8483	*0 9*	*2 0*	*2 0*	41
Total no of cases		24	46	53	123
Standardised rate at ages 35–59 incl		*0 4*	*0 7*	*0 9*	
C Sedentary grades 35–44	15,190			*0 6*	[illegible]
45–54	24,097	*0 6*	*1 2*	*1·6*	83
55–59	9003	*1 4*	*1 6*	*2 4*	49
Total no of cases		28	45	70	143
Standardised rate at ages 35–59 incl		*0 5*	*0 7*	*1 2*	

See footnotes to table V

A Postmen relatively much physical activity

B Postal and telegraph officers (counter hands), postal super and postmen higher grade intermediate as regards ph activity

C P O telephonists, Civil Service executives and clerks physical activity

χ^2 = 16 27 0 001 < P < 0 01 testing the difference between the t groups of workers in the distribution of the number of among the three types of incidence abels" for coronary heart-disease were collected by special rrangement at headquarters in Whitehall and the General ost Office. Treasury Medical Staff scrutinised and checked he diagnoses by correspondence with hospitals and with men's private practitioners and where possible by personal bservation In two-thirds of the cases there was also record f confirmation of diagnosis by a specialist or a hospital pecial arrangements were made with establishment officers or the reporting of all deaths, in particular those occurring ithout preceding sickness absence and copies of all death ertificates were examined The relevant cases and deaths rom coronary heart-disease, presumably related to atheroma, s well as doubtful cases, were then notified by the reasury Medical Service to the unit

able v amalgamates the available data. There were 37 "first episodes" of coronary heart-disease in a 'population' of about 110 000 men most of whom were tudied for two years, making approximately 180 000 man years of observation The incidence of angina rises o 1 2 per 1000 at 55–59 years of age, of early mortality i.e., of those dying in the first three months) to 2·0 he total incidence to 4 9 per 1000 About a quarter f the cases presented as angina, about 40% died in the rst three months of the clinical disease

Tabulation of this data was not begun until analysis f the figures from London Transport was advanced, nd we were therefore most interested to see whether he *experience of the transport workers was repeated* ostmen alone of the seven grades have a physically ctive job though this is not particularly strenuous, hether *judged by the degree of physical activity* mostly walking with a variable amount of stair climbing ycling and light carrying) or its duration (perhaps a hird of the postmen s duties are in the preparation and orting of mail and parcels and this proportion was reater before the Postman Higher Grade was introuced in 1946)( ) There is the further complication hat all postmen higher grade have been postmen, as ave many of the supervisors However there is no oubt that the physical exertion at work of the postman greater than that of any of the other grades included nd there are three truly sedentary grades for comparison -telephonists, executives and clerks. The three parts f table vi thus represent three descending degrees of hysical activity at work the postmen are the most ctive the telephonists, executives and clerks are edentary; the other three postal grades are *less active* han the postmen and, as they are on their feet much or ost of the time, can be considered intermediate in espect of physical activity between the postmen and the edentary group

The results (table vi) show that the total incidence of oronary heart-disease is *lower in the postmen* than in he sedentary grades. Their case fatality is also lower— third in the postmen (57 of 171) compared with almost half in the telephonists, executives, and clerks (70 of 43) Again, therefore as with the transport workers, he early mortality of the physically active group (0 6) substantially less than that of the physically inactive 1 2 per 1000) On the other hand the incidence of ngina is higher in the postmen than in the sedentary orkers (0·7 against 0 5) These differences between he postmen and the sedentary group obtain for each the three constituent sedentary grades individually each of the three mortality is higher than among the ostmen and the incidence of angina is lower and here is a fairly consistent pattern in each age group The postal grades which are 'intermediate' in respect of physical activity show total incidence and early mortality rates that lie, on the whole, between those of the postmen and the sedentary grades.

The experience of the postal workers and Civil Servants may therefore be said to resemble that of the transport workers the physically active group (the postmen) have rather less coronary heart disease, and what disease they do have is less severe There is a greater tendency for the non fatal cases among the physically active group to take the form of angina pectoris (or to be labelled thus) so that once again as in the London Transport survey the incidence of angina in the active men is higher than in the physically less active men The frequency of the diagnosis of angina is particularly interesting for this survey was on a countrywide basis and involved large numbers of practitioners.

Possible psychological explanations again readily come to mind for these variations in coronary experience, though it is difficult to think of mental stress *common* to clerks, executives, and telephonists, yet absent from the others However that may be, we felt that the main interest of these findings in postal workers and Civil Servants lies in the support they provide for the idea suggested by the observation of the transport workers—that physical activity at work is important in relation to the coronary heart-disease of middle aged men

(To be concluded)

THE
RECOGNITION OF WHOOPING-COUGH

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The following account of whooping-cough in young children is derived from five years study of infective respiratory disease in a thousand socially representative families with infants and young children in Newcastle upon Tyne

The justification for a fresh description of such a common disease lies in the difficulty of its early recognition especially in the first week of the illness when infectivity is high and the need to isolate the infected child from other susceptible children is urgent The difficulty is not openly recognised and will be increased greatly in the future by the modifying effects of widespread preventive vaccination

The diagnosis of whooping-cough still rests in most instances on clinical judgment Pernasal swabbing is unlikely to become an acceptable procedure in domestic practice and even in the expert inquiry by the Medical Research Council (1951) bacteriological proof was achieved in only 58% of the cases diagnosed as whooping cough. For these reasons we first describe whooping-cough emphasising those features which should arouse the earliest suspicion of its presence we next describe its behaviour in 388 children in 1947–52 and finally we consider the validity of our definition and the level of diagnostic accuracy which can be expected from a clinical assessment of whooping-cough

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a) Later in this paper "postmen and sorters are classed for the years 1930–32 as light workers, in comparison with coalminers, for instance and various labourers and craftsmen In the present context the emphasis is on the *relatively* greater physical activity in the work of postmen, compared with the other grades in the Post Office and Civil Service and in particular with truly sedentary workers such as clerks.

Clinical Picture

In most children the first symptom of whooping-cough is a cough For the first few days this is short and "tickly," causing no distress to the child and arousing no suspicion in the minds of the parents The apparent innocence of the early cough is supported by the presence in many children of a nasal discharge, and it is simply regarded as the start of a "cold." In almost half the cases, however, there is no nasal discharge at all. The nasal discharge, once developed, remains watery or mucoid, and tends to wane as the child enters the second week of whooping-cough, whereas the cough, which has grown imperceptibly more pronounced, changes it now comes in bursts or paroxysms In "bronchitis" the child feels the need to cough and takes a breath in anticipation, whereas in whooping-cough he is taken unawares, his chest tightens, and the air is expelled in a sharp rapid stutter

As the second week moves on into the third, the cough increases in speed and rises in pitch, and the paroxysms grow longer and more intense During the paroxysm each inspiration is preceded by a rapid succession of expiratory hacks The child goes red or even blue in the face, the eyes water, saliva and mucus drool from the mouth, and the repeated spasms may end in a strident whoop To complete the distress, many of these episodes are associated with the vomiting of ropy mucus or recent food In a few children the burst of coughing is either replaced or followed by violent and persisting sneezing The spasms often appear to be more severe, and are sometimes more frequent, during the night During the day they are often initiated by excitement or anger, feeding or activity The congestion of the face may be so intense as to cause conjunctival hæmorrhage and epistaxis

In spite of the severity of the cough the general disturbance of the child's health is surprisingly small Although sometimes there is a sharp loss in weight and occasionally frightening emaciation, most of the children simply become indifferent to food and lose a little weight for a week or so at the height of the disease

The dramatic nature of the cough is in striking contrast to the lack of physical signs in the chest In the first two weeks signs are often completely absent, and even at the height of the disease may be limited to a few basal rhonchi In a minority there is a striking bronchitis, and where there is lobular or segmental collapse of the lung, râles will also be present Wheezing is notably absent at all stages of whooping-cough even in asthmatic children Though the bowels may open at the height of a paroxysm, diarrhœa is rare, even in infants, and then it is usually associated with diarrhœal illness in the family or intercurrent infection in the affected child

Gradually, between the fourth and eighth weeks, the coughing spasms grow less, vomiting ceases, and the cough loses its violence and then reluctantly takes its leave However, for weeks or even months after the illness, the cough associated with fresh respiratory infection may closely resemble whooping-cough, although there is no true return of the disease

This, in essence, is the traditional picture We have described it afresh because we have found that the pattern is constant and can be recognised in almost every case There is, however, a wide variation in the tempo of whooping cough and in the intensity of the symptoms, even within the same family We find that the severity is most efficiently assessed not by a count of the daily paroxysms alone but by close attention to the whole clinical picture Where the spasms are few, vomiting occasional, whooping absent, and the constitutional disturbance slight we regard the child as mildly affected, where the paroxysms are many and violent, with frequent vomiting and whooping and loss of appetite, weight, and zest we regard the child as severely affected The group between these two extremes we consider of "moderate" severity Yet, in spite of these variations in degree, the distinctive pattern and movement of the illness can be recognised in the mild as in the severe

Diagnosis

The clinical constancy of whooping cough will permit a clinical diagnosis to be reached in most cases. If we remember to ask, a history of contact is forthcoming in about half the children, and any cough occurring in an exposed susceptible child from ten to sixteen days after exposure should be regarded as whooping-cough until the natural history of the ensuing illness proves the assumption to be wrong

The main problem in diagnosis lies in the separation of early whooping cough before the characteristic cough has developed and whooping-cough which remains mild throughout, from the varied assortment of colds and coughs which are so common in childhood

The condition most likely to be mistaken for whooping cough is the severe cold with an irritating postnasal discharge The discharge in a severe cold is not thin and watery but generally thick and purulent, often with nasal obstruction, sniffing, and snoring The cough, too, is more noisy than early whooping cough, and comes on particularly at night after first going to bed and on rising in the morning It is a booming or barking cough, and though it may last for several weeks it does not change its character or progressively increase its speed and intensity

The next problem in diagnosis is to distinguish whooping-cough from that group of diseases covered by the broad label of "bronchitis" In our experience bronchitis presents in three main ways as an extension of the severe cold which we call "coryzal bronchitis" as a sharp respiratory illness, an "acute bronchitis" with constitutional upset and widespread rhonchi in the chest, and as respiratory illness dominated by wheezing which we call "wheezy bronchitis" The last category will naturally include children who have asthma, but most wheezy bronchitis is probably infective

With careful attention to the cough, the physical signs in the chest, and the progress of the disease in the first ten days, the separation of these three conditions from whooping-cough is not difficult When a severe cold goes on to a coryzal bronchitis, the cough often becomes loose or rattling but does not increase in speed and is not associated with choking or with vomiting The chest will be full of rhonchi, in contrast to the pulmonary silence so characteristic of the early days of whooping cough

Acute bronchitis is quite a different illness, with a sudden onset and a rapid tempo A watery nasal discharge may precede the cough but rarely for more than twenty-four hours With this mild rhinitis there is sometimes a sore throat, and the voice may be hoarse The cough is generally hard and barking In the infant and younger child wheezing is not uncommon, and this in itself is sufficient to exclude whooping-cough Although vomiting at the onset of acute respiratory illness is common continued vomiting is unusual—a fact which is true for almost all respiratory diseases apart from whooping cough

The disturbance of general health in acute bronchitis develops rapidly and is at its height towards the end of the first week The whole illness is generally over within two or three weeks

Since wheezing is so unusual in whooping-cough, the distinction between it and wheezy bronchitis presents little difficulty

As the characteristic cough of whooping-cough develops, the idea of a foreign body in the bronchi or of primary lung tuberculosis may arise These mportant conditions however are rarely mistaken for whooping-cough and their special features will not be lescribed here.

A distinction between pertussis and parapertussis is mpossible without bacteriological help Though parapertussis can present as a mild whooping-cough, it may produce no more than a modest cold and cough or bronchitis lasting less than a month However it forms a small and unimportant part of the total picture of whooping-cough and need be considered only when second clinical attacks of whooping-cough occur in the same child.

Epidemiology and Character of Whooping cough in Newcastle upon Tyne

Amid the bewildering variety of respiratory diseases we have accepted as whooping-cough any illness in which the child developed a rapid spasmodic choking cough generally associated at some stage with vomiting and less often with whooping and lasting for a month or more. Since symptomless carriers are almost unknown this clinical definition can be completed for the small atypical minority by accepting in addition any respiratory illness in which *Hæmophilus pertussis* can be isolated from either the respiratory tract or its discharges

On the basis of this definition 388 (43%) of 906 children studied from birth until either their 5th birthday or their death had whooping-cough, and 97 (11%) had whooping-cough before they were a year old Whooping cough is most dangerous, though not always severe, in infancy The 6 children with pneumonia and the 3 with fatal whooping-cough were all infants and there were no deaths after the first year The main features of whooping cough in infancy were as follows :

		No of cases (%)
Cough		100
Vomiting		74
Whooping	55	93
Choking alone	38	
Nasal discharge		49
Anorexia		45
Loss of rest		43
Diarrhoea		
Pneumonia		6
Death		3

There were additional features affecting the group as whole which will now be mentioned because they bear directly on the recognition of whooping-cough Fig 1 shows that unlike measles, whooping-cough was continuously present throughout the five years without epidemic peaks. For the doctors of Newcastle there were no close seasons, and they could expect to meet whooping cough at any time Again, there was no exemption for the young infant The first affected child was only 14 days old, and 5% of the whole group had started whooping cough before they were 6 months old Fig 2 shows the steady progress of whooping-cough through these 906 children year by year

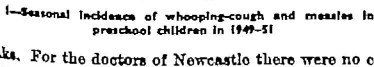

Fig 1—Seasonal incidence of whooping-cough and measles in 906 preschool children in 1949–51

Again the source of the whooping-cough was known or strongly suspected in more than half the children and inquiry for a history of contact is a valuable and, we suspect, often neglected procedure

When contact took place within the family circle, infectivity was high, 8 out of every 10 of the survey children who were susceptible contracting whooping cough In 18 families the whooping cough also spread to one or other of the parents, producing a mild or moderate attack, and 3 mothers appeared to be the first affected members of the household

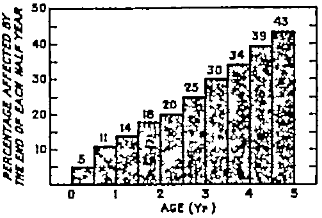

Fig 2—Progression of whooping-cough through 906 preschool children in 1947–52.

Discussion

We have described whooping cough as we have seen it in 388 young children and their families The clinical concept of whooping cough that grew out of our total experience of respiratory illness in the 906 families and led to our accepting these 388 and rejecting others has already been defined

We must now consider the reliability of our definition —how far we have included children who really had colds or bronchitis and how far we have excluded atypical examples of genuine whooping-cough. The level of diagnostic accuracy which can be expected in a clinical survey of this kind is so important that we shall set down the reasons why we regard our definition of whooping cough as essentially reliable

In 278 (72%) of the affected children there was confirmatory evidence from known contacts or from secondary cases developing within the family

Again, among the 388 children only 4 had a second attack during the five years Let us suppose that in a substantial proportion of our accepted cases the diagnosis was false and they had some clinically similar respiratory disease which gave no immunity If we take the extreme view that none were correctly diagnosed, the number of children with one, two or more attacks would approximately follow a predictable distribution In our total group of children the number of colds experienced in the first year of life did follow this type of distribution very closely ; and if this applied to the children with whooping-cough we should have expected not 4 but 98 second attacks, together with 17 third or later attacks

We have naturally considered the children with double attacks with great care If we assume that these were due to infection by *H parapertussis* the minimal incidence of that disease in our total picture of whooping cough was 1% which is almost the figure found in the Medical Research Council's (1951) investigation As regards the lower limit of true incidence, therefore we feel confident that we have not overestimated the figure

But we are still faced with the possibility that whooping-cough is not a consistent disease, and that by definition we have been seeing only the centre of a clinical spectrum and missed a wide marginal band of atypical cases. Our reluctance to attempt intensive bacteriological investigation over a wide range of respiratory disease does not allow us to give a bacteriological answer to this important question. Some help on this point however was given in the course of the Medical Research Council's (1951) inquiry Dr W C Cockburn (personal communication) and his colleagues found that, in 836 children who developed clinical whooping-cough, *H pertussis* was recovered from the nasopharynx in 58%, whereas in 380 children who were exposed to whooping-cough and developed a non paroxysmal cough from 7 to 42 days afterwards the organism was recovered from some 5% Since this was a group of children in which we would expect to find the atypical cases of pertussis, the marginal fringe throughout the general child population must be very small 388 (43% of our total group) had therefore experienced a disease which we feel sure was whooping-cough by their fifth birthday

Comparisons with the notifications of whooping-cough in Newcastle over the same period are interesting From 1947 to 1951 there were 3624 notifications in an estimated average population of 24,500 children aged less than 5 years This means a notified incidence in the preschool child of 15%, or a third the observed incidence in our representative group There are several possible reasons for this discrepancy only three quarters of our children with whooping-cough saw their family doctor, the doctor, having recognised the disease, does not always notify it, and in some cases the doctor does not recognise the whooping cough and calls the case one of bronchitis We have no exact information of the relative importance of these three factors, but we feel sure that failure of recognition is not the least important

Summary

The present character of whooping-cough in a representative group of families with young children is described

In five years 388 (43%) of 906 preschool children developed whooping cough

Family infectivity was high, and whooping cough followed in 8 out of every 10 susceptible children exposed within the family circle

Although the tempo and severity vary considerably, a constant pattern of illness is present in the great majority of cases, and whooping cough can be strongly suspected in many of these in the first ten days

In this article we are speaking as members of a group of doctors, health visitors, and secretaries engaged in the study of illness in young children This inquiry is directed by Sir James Spence, Dr F J W Miller, and Dr Stanley Walton, the medical officer of health We wish to thank all who shared in this work.

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COUNTER-IRRITANTS

A METHOD OF ASSESSING THEIR EFFECT

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Counter irritation is perhaps the oldest of all methods used for relieving pain The physiological mechanisms responsible for this action have never been satisfactorily defined, but they are discussed in many of the standard works on pharmacology (Poulsson 1938, Goodman and Gilman 1941, Douthwaite 1952, Wilson and Schild 1952) Most workers make a distinction between rubefacients, which cause cutaneous vasodilatation by an axon reflex, and counter irritants proper, which stimulate the sensory nerve endings and produce burning pain. It is well known, however, that the effects depend largely on the concentration of the medicaments · a strong preparation of a rubefacient can cause considerable irritation, and powerful counter-irritants are rarely free from some vasodilator action Irritation often develops within a few minutes, whereas vasodilatation may become conspicuous only after $^1/_2$–1 hour In recent years synthesis of several esters of nicotinic acid has m available a new group of drugs which cause vasodilatat when applied to the skin Their effects probably depe on rapid absorption and a direct action on the blo vessels of the skin These are now in common use counter irritants, either alone or in combination w other substances such as menthol, camphor, and capsi

We report here a simple experimental method assessing the effects of rubefacients and counter irrita especially for determining the efficacy of the esters nicotinic acid in the relief of pain

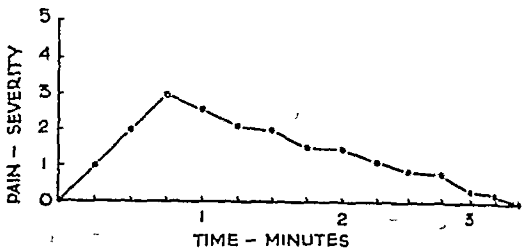


Fig 1—Production of pain with intramuscular saline solution in J. G. (composite graph made from 28 graphs)

Production of Pain

We produced pain of predictable severity and durat by injecting one another intramuscularly with hyperto saline solution The technique has been used by oth

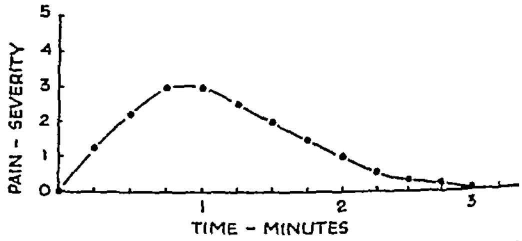
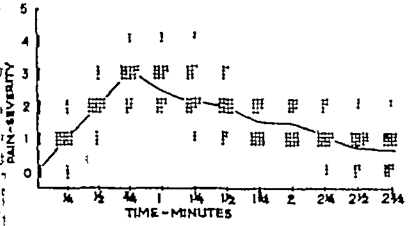


Fig 2—Production of pain with intramuscular saline solution in S (composite graph made from 30 graphs)

especially Lewis (1938) and Kellgren (1949), who re nised its advantages in experimental work becau leads to "a continuous pain which resembles more clo the pain of disease than does the momentary produced by exploration with needles" The techn is therefore different from that of previous workers have studied ischaemic muscle pain (Hower and K 1948) The site selected for the injections was the mu belly of the brachioradialis $2^1/_2$–3 in below the exte epicondyle of the humerus This produced aching p which was most intense at the site of injection but so times radiated down the extensor aspect of the fore as far as the wrist The aching increased in severity the first minute and then diminished progressively had usually disappeared after about three minu While the severity of the pain was being recor movement of the arm was avoided

The earlier tests were made with 6% saline It thought, however, that the pain caused by this con tration might be too severe to be relieved by coun irritants used therapeutically Accordingly experim were made to determine the minimal effective concen tion—i e, the one which would cause pain which relatively mild but nevertheless adequate for recor and constant enough in intensity and duration critical concentration was discovered at 2 75% fo dose of 0 2 ml Solutions only slightly weaker (2 caused negligible discomfort The pain response recorded every 15 seconds An arbitrary system numerals—1, 2, 3, 4—was used to represent increa



g. 3—Production of pain with intramuscular saline solution in J G M (scatter diagram)

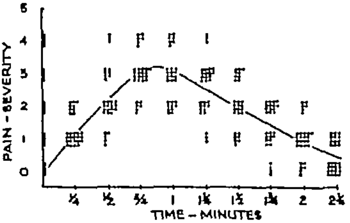
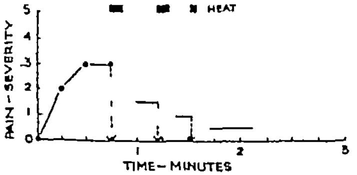


Fig 4—Production of pain with intramuscular saline solution in S.A. (scatter diagram)

verity These numbers have no absolute significance hey provide a useful method for recording a substantial hange—increase or decrease—in a pain characterised y fairly rapid onset and relatively slow deferrvescence sing hypertonic saline as described above an observer oon learns to recognise a pain response which is close o the mean and others which deviate from this But the easurement of pain is necessarily a procedure in which o-one can share; hence it cannot be assumed that the bitrary assessments of pain are transferable from one bserver to another—even under the standard conditions f this experiment The similarity of the control curves f the two observers in the present investigation is herefore a matter of little importance The pattern of hese records (figs 1–4) was sufficiently consistent for ach observer In this investigation upwards of 200 njections of hypertonic saline were given On 4 occasions ne of us (S A) experienced no pain following the njection. It is difficult to account for this exceptional ccurrence, but it may have been due to the placing of he saline solution in an insensitive zone of muscle or—hough this is less likely—in a small vein When another njection was given a few minutes after these failures,' ching pain of the usual intensity was felt in the forearm

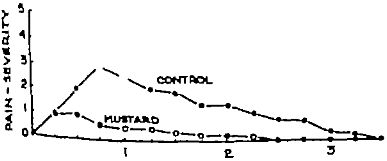


g. 5—Radiant heat as counter-irritant (J G M 16 tests S. A. 13 tests no failures)

Physical Counter Irritants

As a preliminary to studying the effects of chemical ritants applied to the skin in ointments, an attempt was ade to produce counter irritation with radiant heat nd with continuous galvanism.

Radiant Heat.—As a control test saline solution 2 75%) was injected into the brachioradialis muscle of one arm and the resulting pain was recorded. After 10–15 minutes a similar injection was made into the other arm and immediately the forearm—especially the extensor surface—was held close to an electric radiator so that fairly severe burning pain was felt in the skin The result was that the aching pain from the intramuscular injection of saline was completely abolished. The number of tests made was 29 and the same result was invariably obtained (fig 5) It was also found that if the injection of saline solution was made into one forearm and the other arm was simultaneously exposed to strong radiant heat the severity of the aching pain was greatly relieved but not entirely abolished.



g. 7—Volatile oil of mustard as counter-irritant in J G M (composite graphs from 21 consecutive tests and 28 controls)

Continuous Galvanism.—The procedure here was similar to that adopted to test the effect of radiant heat. The indifferent electrode was placed on one arm An injection of 2 75% saline solution was then made into the other brachioradialis muscle and the exploring electrode immediately placed over the belly of the muscle. When the aching pain had developed, galvanic stimulation was rapidly increased to 30 mA This produced in the skin severe irritation burning in quality and only just tolerable, which completely replaced the aching sensation arising from the saline solution (fig 6)

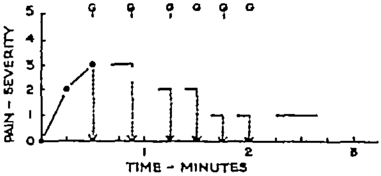


Fig 6—Galvanism as counter-irritant (J G M 17 tests S. A. 5 tests)

Chemical Counter Irritants

The two further series of tests recorded below were made to determine the value of a skin irritant (volatile oil of mustard) and a vasodilator (an ester of nicotinic acid) in relieving muscle pain induced by saline solution

Mustard—The preparation used was 3% volatile oil

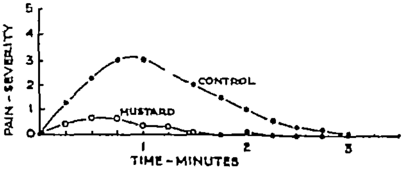


Fig 8—Volatile oil of mustard as counter-irritant in S. A. (composite graphs from 21 consecutive tests and 30 controls)

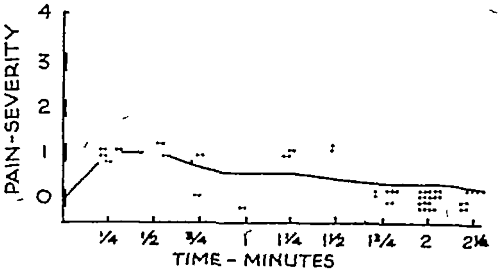


Fig 9—Volatile oil of mustard as counter-irritant in J G M (scatter diagram)

of mustard in simple ointment (*B.P*) A preliminary control test was made by injecting saline solution into one arm as described above, and the intensity and duration of the pain were recorded as previously described The other arm was then prepared by liberal application of the mustard ointment from the wrist to about 2 in above the level of the elbow-joint After about 20 minutes the skin irritation was intense, and was judged to be about as severe as any normal person would be prepared to tolerate Vasodilatation developed slowly at the site of application, but the flushing of the skin was much less intense than that produced by the nicotinates applied locally (see below) At this stage an injection of 2 75% saline was made in the usual way Each observer carried out this procedure on 21 occasions, and the results are shown in figs 7–10 It will be seen that, in the presence of skin pain induced by oil of mustard, much lower levels of deep pain were experienced following intramuscular injections of hypertonic saline

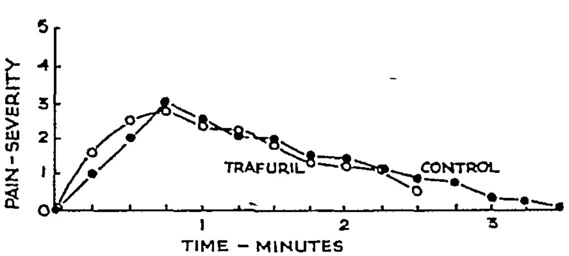


Fig 11—Trafuril as counter-irritant in J G M (composite graphs from 21 consecutive tests and 28 controls)

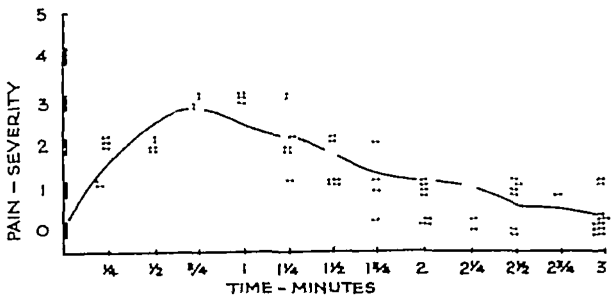


Fig 13—Trafuril as counter irritant in J G M (scatter diagram)

Ester of Nicotinic Acid—When 5% tetrahydrofurfuryl nicotinic acid ('Trafuril') is applied to the skin of the forearm, vasodilatation begins after about 5 minutes and becomes intense in about 20 minutes The flushing of the skin is accompanied by a feeling of warmth and occasionally slight pricking

The same procedure used in testing the effect of volatile oil of mustard was adopted to assess the pain relieving action of trafuril The results are shown in figs 11–14 It is clear that, despite intense vasodilatation in the overlying skin, the severity of saline induced muscle pain was not materially affected.

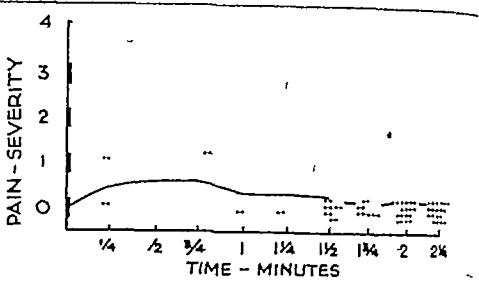


Fig 10—Volatile oil of mustard as counter-irritant in S. A. (sc diagram)

Summary

Hypertonic saline solution injected intramuscul produces deep aching pain Under standard condit the intensity and duration of this pain are const enough to provide a method for assessing the value counter irritants

The phenomenon of counter irritation can be conve ently demonstrated by means of radiant heat or by galva stimulation strong enough to produce severe skin pain

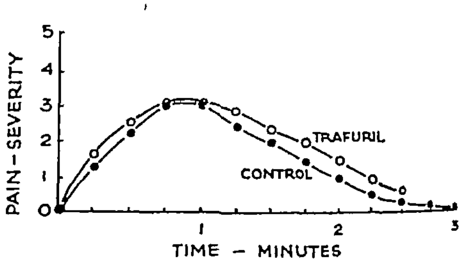


Fig 12—Trafuril as counter-irritant in S A (composite graphs fro consecutive tests and 30 controls)

Volatile oil of mustard (3% in simple ointment), wh causes moderately severe irritation when applied to skin, is very effective in relieving saline induced p Esters of nicotinic acid, in concentrations sufficient cause intense flushing of the skin, are relatively ineffecti

It is concluded that, under these experimental co tions, the relief of deep seated pain by counter irrita depends on the *production* of skin pain of adequ intensity, and that cutaneous vasodilatation is un portant

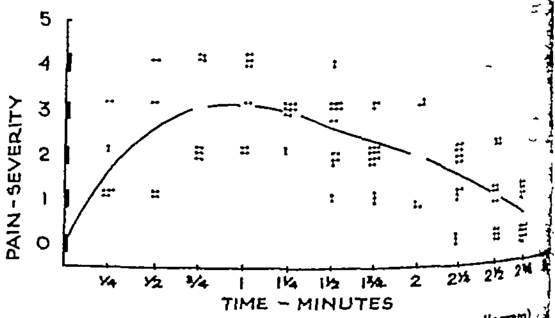


Fig 14—Trafuril as counter-irritant in S A. (scatter diagram)

We wish to thank Miss M Blue, of the physiother department, and Mr D W Blackwood, senior pharma for their assistance, and Mr R Callander for the diagram

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CONTROL OF VOMITING IN CHOLERA
AND ORAL REPLACEMENT OF FLUID

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VOMITING is a major alimentary symptom in cholera second only to diarrhœa in this respect It may be present either from the onset of the illness or may start later when the patient is recovering from dehydration after intravenous transfusions Vomiting was present in 40% of our cases of the 1953 epidemic (437 out of 1093 cases)

The usual remnants of the stomach contents come out at first but subsequently the vomitus is entirely watery The act of vomiting is distressful and noisy and quickly leads to exhaustion and shock

AVOMINE THERAPY

In 59 cases of cholera in the latter part of the 1952 epidemic and in 127 cases during the 1953 epidemic I treated vomiting with tablets containing 'Avomine' 25 mg (14 mg of promethazine base and 11 mg of 8-chlorotheophylline in chemical combination) During the same period 907 cases of cholera were treated without avomine, making a total of 1093

In the mild cases vomiting was often checked with a single tablet. When, however it continued further tablets were given The largest number of tablets found necessary was six in twenty four hours in 1 case The patients to whom it was given were a selected group whose condition was relatively satisfactory but it is noteworthy that there was not a single case among them in which vomiting was not ultimately controlled with avomine. Nor have I observed any toxic or untoward effects with the doses mentioned

The vomiting and the distress it causes are described by Sir Leonard Rogers (1921) thus

> the vomiting of much watery fluid when but little has been swallowed is one of the pathognomonic features of cholera. When very copious it does much to exhaust the patient and may be an important factor in producing collapse On account of the terrible thirst the patient calls repeatedly for water only to reject it almost at once together with any medicine which may have been given. Nothing however is more cruel than to withhold water from those in the throes of cholera

The doctor who sees a cholera patient is often confronted with a dilemma. If he allows water even in small quantities the patient will usually throw it up immediately and the dehydration and shock will increase, thus setting up a vicious circle. If on the other hand the doctor withholds water from a patient with extreme thirst—a distressing thing to do—the dehydration and shock may again be increased. After the administration of avomine however there has been no necessity of withholding water which could be given in any quantity desired.

NUMBER OF AVOMINE TABLETS WHICH RELIEVED VOMITING IN 100 CASES

No. of tablets needed to stop vomiting completely	1	2	3	4	5	6
No. of cases	41	30	18	7	3	1

The numbers of tablets required to relieve vomiting in 100 carefully observed cases of cholera accompanied by vomiting are given in the accompanying table These cases were observed between April 5 1953 and June 25 1953, the seasonal peak of the cholera epidemic

All these patients had agglutinable cholera vibrios in their stools on culture The stool specimens were collected in each case in a sterile test-tube after a boiled no 10 catheter had been passed into the rectum The cultures were made usually within fifteen minutes of collection, on the following three different culture media on separate plates: MacConkey taurocholate agar and D.R.C (Panja and Ghosh 1943)

REHYDRATION

The control of vomiting with avomine makes it possible to relieve the cholera patient's extreme thirst to replace water and electrolytes by mouth and to prevent the loss of body fluid in the vomitus Avomine, however does not check choleraic diarrhœa, and for this purpose I use the juice of the raw leaf of *Coleus aromaticus* an Indian plant (Chatterjee 1953)

When vomiting and diarrhœa have been substantially controlled with these two agents we have found it possible, in the mild cases, to restore the lost fluids and electrolytes by mouth alone, enabling these patients to tide over the condition to convalescence We classified as mild those cases with blood sp gr 1·062 or less and a good pulse there were 33 such cases. In moderately severe cases with blood sp gr 1·062–1·064 administration of fluid by mouth and per rectum was necessary: there were 153 such cases. The fluid used in my ward for both routes was composed as follows:

Sodium chloride 4 g
Glucose, 25 g
Water ad 1000 ml.

After a free flow of urine had been established potassium chloride 2 g was added to each litre of fluid

DISCUSSION

Of 1093 patients 33 with mild cholera were tided over to convalescence by the administration of fluid by mouth alone and 153 patients with moderately severe cholera were cured by the administration of fluid by mouth and per rectum making a total of 186 cases (17% of all the patients treated) in which intravenous or parenteral administration of fluid was unnecessary All 186 patients were discharged clinically cured

A substantial majority of cholera patients are brought to the hospital with advanced dehydration and shock requiring intravenous transfusion therapy But it is possible that if full use were made of avomine to prevent vomiting many of these cases could be saved from drifting into this advanced stage of dehydration and shock The proportion treated without intravenous therapy might well be higher than 17% In our series, as has been explained, avomine was given only to the 186 cases (17% of the total) who seemed likely to benefit

SUMMARY

Vomiting in cholera leads to dehydration and shock

In 59 cases in the 1952 epidemic and in 127 cases in the 1953 epidemic vomiting was treated with avomine Of these 186 cases 33 were mild and 153 moderately severe All these patients recovered

Avomine does not stop the diarrhœa For this purpose the leaf juice of an Indian plant, *Coleus aromaticus* was used.

The combination of these two remedies enabled patients with mild or moderately severe cholera (blood sp gr up to 1·064) to achieve convalescence without intravenous or parenteral transfusions

I offer my heartfelt gratitude to the memory of the late Dr Shyama Prosad Mookherjee who was very keenly interested in our work and I wish also to thank Dr Debi Kumar Bose and Dr Priya Ranjan Chakravarty of the laboratory section and Dr Robi Shaha, of the clinical section of the cholera ward, for their coöperation Messrs. May & Baker supplied the avomine and partly financed this research

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DUPUYTREN'S CONTRACTURE

A RADIOTHERAPEUTIC APPROACH

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Dupuytren's contracture, if left untreated, slowly progresses with an increasing flexion deformity of one or more fingers and accompanying increasing functional disability During the last fifty years many different methods of treatment have been employed, including injections of lysins, electrotherapy, physiotherapy, and psychotherapy, which have all been in vogue from time to time More recently treatment with vitamin E has been introduced, but with somewhat equivocal results, and the treatment of choice has remained primarily by surgery

Treatment by ionising radiations has received but little following, and only the Radiumhemmet in Stockholm (Skoog 1948), and Slanina (1948) in Germany, report on its use in any considerable number of cases

Histopathological Changes

Although Dupuytren's contracture remains of unknown ætiology, much work has been done on the histopathological changes which accompany it, especially by Meyerding et al (1941) and by Skoog (1948)

From earliest times the changes in the palmar fascia have been held responsible for the characteristics of Dupuytren's contracture Workers have emphasised that fibrosis and contracture cause the chief manifestations by contracture of the palmar fascia In a detailed study of this subject, however, Meyerding et al (1941) have shown that changes take place not only in the palmar aponeurosis but also in the " extrafascial " tissues, and that the changes in the skin and subcutaneous tissues are as important as those in the palmar fascia

EXTRAFASCIAL CHANGES

The earliest evidence of histological changes is a lymphocytic infiltration combined with an increase in the number of capillaries This begins in the interstitial connective tissue and gradually spreads to all the tissues in the palm This infiltration precedes fibrosis, fat is absorbed or destroyed, and new connective tissue is formed Then, in advanced cases, subcutaneous adipose tissue and sweat glands become rare or absent, and dense parallel strands of fibrous tissue lie beneath the reticular layer of the dermis Hence the skin becomes thickened, puckered, and bound down to the underlying tissues The accompanying photomicrographs illustrate this " inflammatory reaction " in an untreated case, showing the typical perivascular cuffing, lymphocytic infiltration, and aggregations of fibroblasts (figs 1 and 2)

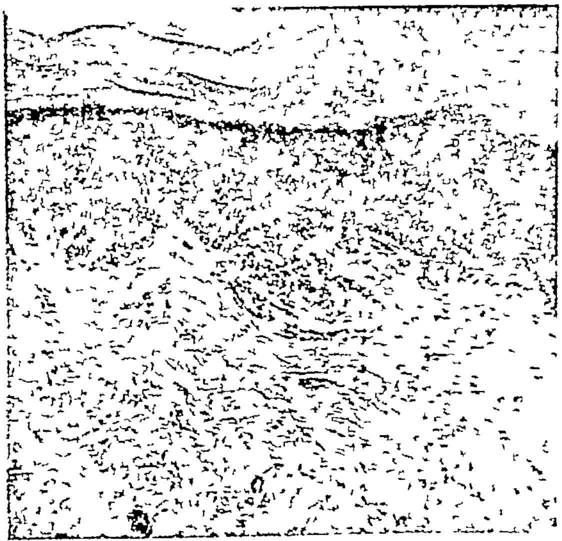

Fig 1—Stage I: nodule in palmar skin of untreated case showing epidermal thickening, with increased vascularity in subepidermal layers aggregations of fibroblasts and perivascular cuffing with lymphocytes and plasma cells (×80)

PALMAR FASCIAL CHANGES

These are entirely different from the extrafascial changes Lymphocytic infiltration, increase in capillaries, and perivascular cuffing are almost entirely lacking. The characteristic change is a proliferation of the fibroblasts in the nodules of the contracture In the earlier immature stages the fibroblasts tend to grow in masses closely packed together A cycle of events then takes place in which there is deposition of collagen fibres, contraction of the collagen, and compression of the fibroblasts, producing an avascular scar tissue and contracture of the fascia

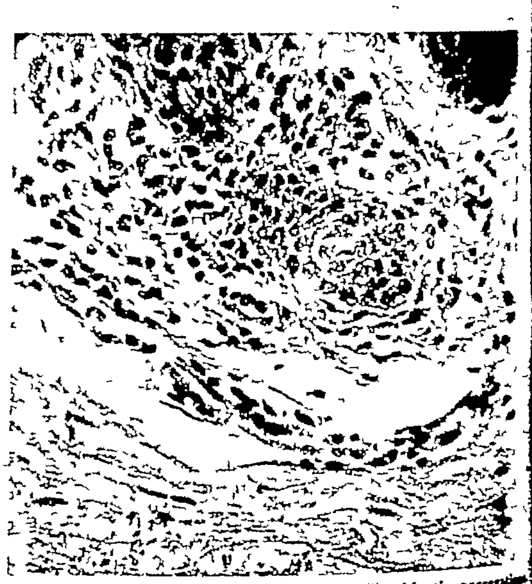

Fig 2—Same section as in fig 1, showing fibroblastic aggregation and lymphocytic infiltration in greater detail (×200).

Skoog (1948) criticises the suggestion that the extrafascial changes are an " inflammatory reaction " and considers that the aponeurosis is the structure where the initial changes occur Furthermore, these changes may become so excessive as to spread beyond the limits of the palmar fascia " in a manner reminiscent of a tumour " This spread progresses diffusely to all parts of the aponeurosis, with the result that changes also take place at the attachment of the aponeurosis to the skin Skoog does agree, however, that in the development of the nodules in the aponeurosis the new formations of connective tissue issue from the perivascular tissue of the adjacent vessels These vessels become dilated, increased in number, and are surrounded by perivascular sheaths of fibroblasts, leucocytes, and round cells, especially in the more mature areas where the round cells predominate

The hypothesis of Meyerding et al (1941) that the skin changes follow an " inflammatory reaction " seems to satisfy the clinical findings of skin thickening, puckering, and nodularity over a wide area of the palm rather than only at the site of skin attachment as postulated by Skoog Moreover, it is well known that skin nodularity and thickening may be found before fascial changes become apparent clinically

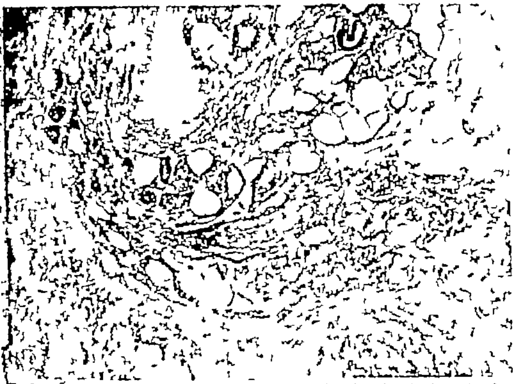

Fig. 3—Stage 3: nodule in palmar skin four months after irradiation showing absence of fibroblastic aggregations and lymphocytic infiltration and no evidence of fat-absorption (×80)

The changes described above can be compared to the changes in scars which become keloid. Glücksmann (1951) has shown that an orderly sequence of events takes place, which he also describes as an "inflammatory reaction." This consists in round-cell infiltration of the subcutaneous tissues, considerable perivascular reaction, and fibrosis—a picture identical with the extrafascial histopathological changes seen in Dupuytren's contracture.

Surgical Treatment

The operation most widely practised today is that based on the lines advocated by Kanavel et al. (1929) consisting of a radical removal of the entire palmar aponeurosis and removal of the affected skin, with skin grafting where necessary. This appears to be satisfactory judged by the early functional results published by various surgeons. However, the recurrence rate following radical surgery is far from negligible.

Reference	*No. of cases*	*Recurrence (%)*
anavel et al. (1929)	39	35
orens (1917–18)	30	33
eyerding et al. (1941)	63	17
avis (1932)	—	30
oss and Annan (1951)	11	10

In view of the histopathological findings described above it is not surprising that the recurrence rate reaches such a high figure, as changes can still proceed in the extrafascial tissues even after the palmar aponeurosis has been excised.

Radiation Treatment

The rationale of treating a condition in which the main emphasis has been on contracture following fibrosis is not at first apparent, but again it is as well to recall the histopathological changes and the close comparison with the similar changes in keloid scar formation. Radiotherapy has been long used in the treatment of keloid and hypertrophic scars, both alone and in conjunction with surgery. According to Levitt (1951) the effect of radiation on the processes leading to the development of the scar appears to be that the round-cell infiltration is reduced or suppressed, probably by direct action. Epidermal fibrosis and proliferation are thus inhibited.

Further, the effect of irradiation on the fibroblasts, as borne out by in-vivo histology and in-vitro experiments, shows that their mitotic cycle can be readily interrupted. The death of the cell will therefore cause a break in the cycle of events so that no further collagen and therefore no further scar tissue will be laid down.

As a result, therefore, of irradiating the whole palm it should be possible theoretically to interrupt the cycle of events producing further contracture. This appears to be borne out both by the accompanying photomicrographs (fig. 3) from cases treated by radiotherapy and by the over-all results.

Staging

In the present series of cases the clinical condition was "staged" according to a modification of the lines advocated by Shaw (1951) as follows:

Stage 1 includes (*a*) hands with a nodule in the palmar fascia not yet including the skin and causing no contracture of the fingers, or (*b*) nodules present in the skin with no apparent changes in the palmar fascia.

Stage 2 comprises a nodule in the fascia involving the skin but not causing finger flexion deformity.

Stage 3 comprises a nodule in the palm invading skin plus flexion contracture of one or more fingers.

Stage 4 includes all stage-3 cases in which the secondary changes have occurred in the tendons or joints of one or more fingers.

Technique

Gamma radiation alone was used in the present series. As the pathological changes may extend throughout the whole of the aponeurotic area the tendency has been to irradiate the whole of this volume of tissue comprising the palmar fascia and adjacent tissues. Two techniques have been used according to the stage of the condition.

In stages 1 and 2, before contracture has

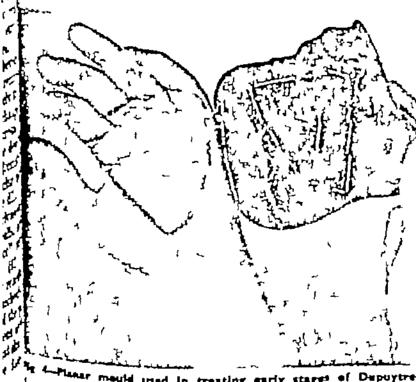

Fig. 4—Planar mould used in treating early stages of Dupuytren's contracture showing area irradiated

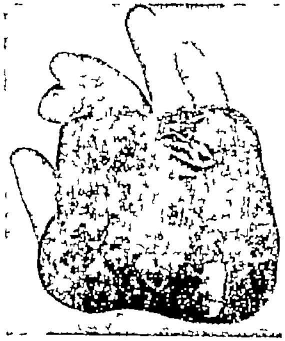

Fig. 5—Planar mould in position for treatment.

occurred, a planar mould is made of Black Tray compound, and the area to be irradiated is mapped out on the mould A treating distance of 1 0 or 1·5 cm is used The mould is illustrated in figs 4 and 5

In stages 3 and 4, when contracture has occurred and a planar mould can no longer be applied, a grip cylinder is made—again of Black Tray compound of a radius of 1 0 or 1 5 cm This is illustrated in fig 6 The total dose of 3000 r to the skin is given in fractional doses of eight hours a day for eight days

Results

The results in 25 cases treated by radium mould technique are given in the accompanying table

In no case did the patient have difficulty in wearing or in retaining the appliance Apart from some skin dryness and occasional slight erythema, no skin reaction was observed in any of the cases thus treated

Subjective improvement—including softening of the nodules, lessening of paræsthesia, and increase in finger movement—were evident within the first four weeks after treatment Objective improvement, gauged by increase in movement, began on an average within 1 7 months and became maximal by 6 0 months There was no improvement after twelve months had elapsed from the time of treatment

The period of follow up was two to ten years Of the 25 cases 75% were improved and 25% remained static Of those cases which improved 25% fully recovered, 25% partially recovered, and 25% were only slightly improved, but in no case was the condition made worse or did the contracture increase after the treatment had been given

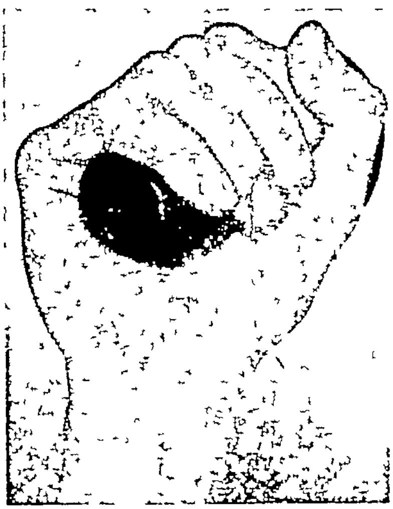

Fig 6—Cylinder or grip mould used when contracture has already taken place.

Those cases in which full recovery occurred belonged to stage 1 or 2, i e , before fibrosis or scar tissue had been laid down

Those cases in which no change, or only moderate improvement, took place belonged to stage 3, when scar tissue had already been laid down and which would only respond to a limited degree, depending on the amount of avascular scar tissue present

These results are confirmed by the findings of Stockholm Radiumhemmet, where, in treating 149 cases, it was found that, although improvement varied considerably, *in all cases the processes were arrested*

The logical approach to the treatment of Dupuytren's contracture appears therefore to be by radiotherapy used either alone or as a preoperative measure If a combined attack be decided on, the functional improvement is allowed to continue until the greatest effect has resulted After this, if functional disability remains, this may be corrected by surgical means Postoperative recurrence will thus be reduced to a minimum

Summary

The results of treating 25 cases of Dupuytren's contracture with radium are reviewed

RESULTS OF TREATING 25 CASES OF DUPUYTREN'S CONTRACTURE BY RADIUM MOULD TECHNIQUE

Case no	Stage	Functional improvement	Time of first improvement (mos)	Time of greatest improvement (mos)
1	3	+ + +	2	6
2	3	—	—	—
3	2	+ + +	1	[illegible]
4	3	+ +	1	1
5	2	+ + +	2	3
6	3	—	—	—
7	2	—	—	—
8	3	+ +	2	5
9	3	+ +	3	6
10	3	+	4	6
11	3	+ +	2	3
12	3	+ + +	1	6
13	1	+ + +	1	6
14	3	+ +	1	12
15	3	+ +	3	12
16	3	—	—	—
17	3	+ +	1	4
18	1	+ + +	1	6
19	3	—	—	—
20	3	—	—	—
21	3	+	1	5
22	2	+ + +	1	6
23	3	+	3	1
24	1	+ + +	1	3
25	3	+	1	3

Average time of first improvement 1 7 mos.
Average time of greatest improvement 6 0 mos.

+ + +	full functional recovery
+ +	functional improvement but short of return to normality
+	limited improvement only
—	no change

The treatment of Dupuytren's contracture by irradiation can be as successful as radical surgery in curing the condition, especially in the earlier stages of the disease. In the later stages improvement is less evident, but in 25 cases in the present series the progress of the disease was arrested

Recurrence following adequate irradiation of the palm appears to be rare, if it occurs at all

Improvement in contracture is maximal within twelve months following the initial treatment

There therefore seems to be a place for a combination of preoperative irradiation followed by radical surgery in these cases, along the lines used in the treatment of keloid scars In these cases complete excision of the aponeurosis can be undertaken without fear of recurrence

The present cases were all treated at the Liverpool Radium Institute, and I am grateful to the medical director Dr J Fulton, and Dr M A C Cowell for their help and encouragement I should also like to express my thanks to Miss D of the statistical department, and Mr W Braden and Mr M Tillp, of the photographic department

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From the Renaissance onward developments in medicine illustrate the extreme difficulty that man has always had when accumulations of facts, the raw data of science, so overload the intellect that logic goes flabby from overwork in systematizing knowledge Imagination is shackled, perhaps by fatigue or by not having the time needed for meditative gestation In any event, we have seen the stringency of the austere rationalism of the Middle Ages and the old urbanity of Greek rationalism fade out before the immense and monolithic aggregations of contemporary fact How truthful were the words of Artemus Ward—'The researches of so many eminent scientific men have thrown so much darkness upon the subject that if they continue their researches we shall soon know nothing' "—Dr W BENNETT BEAN, *Arch intern Med* 1953, 92, 153

PROLONGED APNŒA FOLLOWING INJECTION OF SUCCINYLDICHOLINE

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SEVERAL cases of prolonged apnœa following injection (the ultra-short-acting relaxant succinyldicholine loride have now been published At first this was tributed to possible synergism with thiopentone arron 1952), acidæmia (Harper 1952) respiratory pression due to premedication and thiopentone com ned with hyperventilation (Richards and Youngman 52 Barron 1952) and overdosage with succinyldicholine oldes 1952) The breakdown of succinyldicholine by iolinesterases was demonstrated by Bovet-Nitti (1949) d Bourne, Collier, and Somers (1952) and Evans, Gray hmann, and Silk (1952) found significantly lowered rum pseudocholinesterase levels in patients who recov ed unusually slowly from succinyldicholine Evans al. (1952) also showed that the duration of apnœa llowing the administration of succinyldicholine was proximately inversely proportional to the serum eudocholinesterase level. Bourne et al. (1952) and vans et al (1952) therefore suggested that succinyldi oline should not be given in liver disease severe æmia, or severe malnutrition or after poisoning by mpounds such as insecticides or weed killers, where e serum pseudocholinesterase level might be expected be low Reid and Neill (1952a) recorded two cases apnœa lasting 75 minutes in which the sum olinesterase level was not significantly lowered but ter they found in other cases that the pseudocholin terase levels were considerably depressed (Reid and ill 1952b)

Hall, Lehmann and Silk (1953) who studied the effect succinyldicholine in dogs, suggested that succinyldi oline formed a stable combination with true cholin terase but an unstable one with pseudocholinesterase he combination of pseudocholinesterase was unstable cause the combination led to the hydrolysis of suc nyldicholine; this made more pseudocholinesterase ailable to receive *succinyldicholine*, which was trans rred from its stable combination with the true cholin terase. Evans et al. (1953) demonstrated that the ministration of pseudocholinesterase in purified form ortened the duration of action of succinyldicholine in an, and that it was able to terminate pre-existing nœa There is thus no doubt that the pseudocholin terase level plays the most important part in determin g the duration of apnœa. However it is as well to member that other mechanisms—e.g., central depres on and changes in electrolyte balance and in excitability nerves and muscles—may produce long-continued nœa after succinyldicholine, even if the pseudo olinesterase level is normal. It must have been such ses which had their effect reversed by the administra on of calcium (Mayrhofer 1952) and nikethamide Barron 1952) and play a part in the prolonged effect casionally seen after decamethonium a drug in whose imination pseudocholinesterase has no part.

It is clearly of practical importance to be able to retell which patients are likely to have an abnormally w pseudocholinesterase level. The significance of liver amage undernourishment or cachexia, and previous contact with cholinesterase inhibitors, has already been considered. Several cases have been reported however in which none of these factors seem to apply; the patients appear to be in good health yet they show prolonged reaction to succinyldicholine and a correspondingly low pseudocholinesterase level. Bourne (1953) describes such a patient who on two successive occasions showed prolonged reactions and had an abnormally low pseudocholinesterase level whereas other liver function tests gave entirely normal results. Bourne also refers to a case reported by Davies (1952) in which a healthy militiaman had a pseudocholinesterase level below measurable limits: "Care was taken with this individual to exclude the possibility of his having been in contact with any anti-cholinesterase substance."

In view of these findings the following case may be of interest

Case record

A man, aged 20 was admitted with ten hours history of pain in the left loin He was a Cypriot and his lack of knowledge of English made accurate history taking difficult.

On examination he was apyrexial but flushed, with a white *moist tongue, and tenderness and guarding in the left loin* His heart and lungs were normal, and rectal examination revealed no abnormality Left-sided pyelitis was diagnosed provisionally because the urine looked cloudy and thick A blood-count showed Hb 15·7 g per 100 ml. and white cells 10 000 per c.mm (neutrophils 84%, eosinophils 1%, lymphocytes 14%, monocytes 1%) Mid-stream urine contained some red blood-cells

Treatment — Sulphatriad therapy was begun Intravenous pyelography six days after admission showed poor detail of the calyces on the left side It was therefore decided to cytoscope and examine the patient under anæsthesia.

Premedication was with Omnopon gr $^1/_6$ and atropine gr $^1/_{150}$

Operation —Anæsthesia was induced on the operating table with thiopentone 350 mg (sleep dose) followed by succinyldicholine-chloride dihydrate ('Scoline') 50 mg through the same needle An oral airway was inserted as soon as the jaw was relaxed, and the patient was insufflated with nitrous oxide and oxygen 5 2 litres, no carbon-dioxide absorber being used Cystoscopy and rectal examination were done under satisfactory conditions in about 5 minutes.

As there was no sign of returning respiration at the conclusion of the operation, the patient was taken into the anæsthetic room. There insufflation with pure oxygen (without absorber) was continued for a further 35 minutes, with occasional pauses to see if spontaneous respiration was returning At the end of this period respirations returned, feebly at first and gradually improving during a further ten minutes. The eyelash reflex was now present, but the patient tolerated his airway His condition was deemed satisfactory for return to the ward. On return to his bed he moved a little and tried to remove his airway This was done for him and he nodded his head when asked whether he was all right; he spoke in a slight whisper During the period of insufflation with oxygen his pulse and colour remained satisfactory There was no sign of consciousness. When he was questioned an hour later he said he had regained consciousness during insufflation in the anæsthetic room. He remembered hearing the anæsthetist talking over him but could not understand all that was said He wanted to say that he could not breathe but he could neither move nor speak. He felt air hunger when ventilation was suspended *occasionally He remembered being wheeled back to the* ward and being put into bed

Subsequent Examination and Interrogation.—The patient, a fit muscular young man said that he had been healthy all his life He had never had occasion to see a doctor before his admission to hospital. He had not had previous attacks of jaundice or malaria, and he had no history suggesting amœbic dysentery His present occupation was that of waiter; before leaving Cyprus he worked as a farmer So far as could be ascertained he had not been in contact with any anticholinesterase chemicals.

His blood pressure was 140/85 mm. Hg No physical abnormality was found on re-examination. The pseudocholinesterase *level* was 18 units (normal 51–125) Other liver function tests gave normal results.

As failures of liver function without obvious causes are sometimes due to inherited errors of metabolism, it was decided to investigate the patient's relatives A brother living in this country was quite fit, weighed 157 lb, and had had no illness but appendicitis His pseudocholinesterase level was 8 units, other tests for liver function gave normal results Two siblings, living in Cyprus, were said to be congenitally deaf and dumb

Discussion

There was no indication in the patient's or in his brother's general condition suggesting any debility which might predispose to a lowered pseudocholinesterase level That the increased sensitivity to succinyldicholine was due to this cause is demonstrated by the fact that the patient recovered consciousness during insufflation with oxygen—i e, thiopentone had been metabolised or redistributed. The premedication was unusually light, acapnia was a most unlikely cause, for an absorber was not in use (Bourne 1953) It was impossible to distinguish this patient, when conscious and paralysed, from a fully anæsthetised patient This fact shows the necessity of supplementing oxygen with nitrous oxide during insufflation, as suggested by Bourne

Although the presence of a low pseudocholinesterase level in siblings does not prove that the condition is familial, it is noteworthy that there are other apparently genetic abnormalities in the family

The two brothers were Cypriots, and of three other people in whom we (H L and E S) found an unexplained low pseudocholinesterase level, two were of Mediterranean stock, one being an Italian and the other a Jew Unfortunately it was not possible in either case to examine the blood of relatives

In view of these findings we feel that further cases of sensitivity to succinyldicholine should be published, and if a low pseudocholinesterase level is found which cannot be explained by disease, malnutrition, or poisoning, their families should be investigated for a hereditary or racial basis of abnormally low pseudocholinesterase level

Summary

Apnœa lasting 40 minutes followed the administration of 50 mg of succinyldicholine chloride to an adult Cypriot There was an unexplained low pseudocholinesterase level (18 units)

A brother of this patient also had an unexplained low pseudocholinesterase level (8 units) The possible significance of this finding is discussed

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" The Chadwick battle for mains and drains is read of with surprised amusement by those few who study his life but there is still much hard work ahead for those who believe that money spent on the prevention of disease will pay a far higher dividend than money spent on the cure of a disease already established It is a sobering thought that a week's fog in London can cause more deaths than were attributable to cholera in the great epidemic of 1854 The administrative mind finds it difficult, however, to see far beyond a hospital with all its elaborate mystique of diagnosis and treatment The object of medicine must be to reduce the number of hospital beds needed in the country for the sick, not to increase them Not only is this the right humane outlook but it is also sound practical economics "—*Times Literary Supplement*, Oct 6, 1953 p 1

TORULOSIS*

A CASE MIMICKING HODGKIN'S DISEASE AN RODENT ULCER AND A PRESUMED CASE OF PULMONARY TORULOSIS WITH ACUTE DISSEMINATION

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Fungus infections other than those of the skin mucosæ are seldom recognised in Britain, where the d seated mycoses, except actinomycosis, are often thou of as exotic curiosities unlikely to be met with in practi But there is evidence that they are not as rare here has been believed, and growing awareness of the po bility of their occurrence may encourage their recogniti Thus 8 cases of torulosis, recognised in this count have been recorded (Smith and Crawford 1930, Greenfi et al 1938, Blair 1943, Magarey and Denton 19 Daniel et al 1949, Galton and Whittick 1950, Tay 1953) and the diagnosis of histoplasmosis† has be made in Britain on at least 11 occasions, with mycologi proof in 5 cases (Derry et al 1942, Robb Smith 19 [the case mentioned by Duncan 1945, 1946–47], Lock et al 1953, Symmers 1953) and with less certainty the cases of Arblaster (1950), Crofton (1950), Lamei (1951), and Hutchison (1952)

Since 1946 I have seen 6 cases of torulosis, 2 of his plasmosis, and 1 each of pulmonary blastomyco sporotrichosis, mycetoma, pulmonary aspergillosis, meningocerebral mucormycosis In the same per I have seen only 2 cases of actinomycosis The organ were recognised in the tissues in each case and cultured in all but 4 cases, in which they were identi as cryptococcus, blastomyces, aspergillus, and mucor their histological appearances The patient with my toma was an Arab immigrant from Aden the oth were Europeans normally resident in these islan although all except the patients with sporotrichosis mucormycosis and 2 of those with torulosis had be abroad 4 of the cases of torulosis were straightforwa examples of cryptococcal meningo encephalitis, 2 other cases were unusual and are described here.

Cox and Tolhurst (1946) have given a full account torulosis, of which more than 200 acceptable cases h been published during the fifty-nine years since B (1894, 1895) and Buschke (1895) reported the first cert case (mycologically proved by Benham 1935), o such published observations as are specially pertinent the following cases need be referred to here

The First Patient

CASE RECORD

A mechanic, born in 1920, noticed painless lumps in left side of his neck in July, 1947 His health had excellent until then, apart from mild attacks of ma during military service in Burma and Ceylon from 194 1945 By November, 1947, enlarged lymph nodes palpable in each side of his neck and in the left axilla. Ra graphy of the chest showed enlarged hilar lymph ill-defined opacities in the middle zone of the right lung thought to be tuberculous No tubercle bacilli were in his sputum Biopsy of two nodes from the left n December 1947 was said to show Hodgkin's disease (see below) The patient's general condition was so good that he refused all treatment. He was next seen in March 1949 complaining of tiredness and productive cough during the preceding few months Enlarged lymph nodes, up to 3 cm. in diameter were present in the neck armpits, and right groin and the edge of the spleen was palpable 3 cm below the costal margin radiography of the chest did not show any change Blood: 4 310 000 red cells per c.mm Hb 9·4 g per 100 ml; leucocytes 5900 per c.mm (neutrophils 82%, eosinophils 1%, lymphocytes 7% monocytes 10%); platelets 73 000 per c.mm. On April 5 1949 he was admitted to the Queen Elizabeth Hospital Birmingham for deep X-ray therapy

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* In conformity with the recommendations of the Medical Committee of the Medical Research Council (M.R.C. randum no 23 1949) the name torulosis is used in this to denote the disease caused by *Cryptococcus* , (Sanfelice) Vuillemin.

† Locket et al. (1953) refer to a patient with histoplasmosis in South Africa, who died shortly after arriving in this Atkinson (1953) confirms that this was the case by Cunningham and Garrod (1950) and recorded by and Brandt (1951)

First Admission

From April 8 to April 22 a total dose of 1000 r each was given to right and left cervical fields both axillæ and anterior and posterior thoracic fields, and of 600 r each to anterior and posterior splenic and right inguinal fields Throughout his stay in hospital the patient had irregularly intermittent pyrexia up to 103·0°F (39·8°C); malaria parasites were not found He was discharged home on May 8 The response to therapy seemed to be disappointing because his general condition had improved little although the spleen and superficial lymph nodes were no longer palpably enlarged. Radiography of the chest showed no change

Progress

By May 27 1949 there was unexpectedly great improvement; the patient felt perfectly well and had had no fever since leaving hospital On Jan 6 1950 he coughed up a little bright blood radiography showed extensive opacities in the right lung and deviation of the mediastinum to the right. In March 1950 two small painless ulcers appeared on the face, one in front of the right ear at the site of an abrasion while shaving and one on the nose where he had accidentally scratched himself with a finger nail These lesions were thought to be typical rodent ulcers and on April 14 the preauricular one was excised histological examination showed that it was a cryptococcal granuloma The patient was readmitted to the Queen Elizabeth Hospital on May 6

Second Admission

The ulcer (1·0 × 0·8 cm.) on the nose (fig 1) had a slightly moist yellowish red base and a low rolled pearly edge surrounded by an ill-defined cyanotic corona 0·25 cm wide There was now a similar lesion, 0·8 cm. in diameter on the left side of the chin, which had also followed a razor-cut The scar following excision of the preauricular ulcer was healthy No other skin lesions were found. There was no lymphadenopathy and the spleen and liver were not palpable; the lower half of each lung was dull to percussion, and there were râles at the right base the other systems were normal

Investigations

Cryptococcus neoformans was isolated from the ulcers sputum, and urine; the urine was otherwise normal and the feces were normal Tubercle bacilli were not found in the sputum or elsewhere at any time during his illness. Intradermal tests with histoplasmin were negative Serum Wassermann and Kahn tests negative Lumbar puncture: clear colourless cerebrospinal fluid (C.S.F.) under a pressure of 120 mm. C.S.F. no block protein 20 mg per 100 ml (no excess of globulin) reducing substances 58 mg per 100 ml., and chloride (as NaCl) 700 mg C.S.F. blood and sternal marrow cultures in routine media and on Sabouraud's and beerwort media remained sterile after twenty eight days. Erythrocyte sedimentation rate 19 mm in one hour (Wintrobe) Blood: red cells 4 700 000 per c.mm Hb 11 g per 100 ml; leucocytes 11 800 per c.mm. (neutrophils 87%, eosinophils 1% lymphocytes 8% monocytes 4%) and platelets 319 000 per c.mm. The number of white cells gradually decreased by June 5 to 5000 per c.mm. (neutrophils 71%, eosinophils 3% lymphocytes 22% monocytes 4%) Sternal marrow: no diagnostic abnormality Blood-chemistry: urea 37 mg. per 100 ml., albumin 4·0 g per 100 ml globulin 2·6 g per 100 ml.; free cholesterol 64 mg per 100 ml., ester-cholesterol 70 mg; alkaline phosphatase 27·0 units (Jenner and Kay) van den Bergh reactions negative thymol turbidity test 0·5 units (Maclagan); cephalin-cholesterol flocculation test 1 + colloidal gold curve 12210 Electrocardiograms normal. Chest radiography: mediastinum displaced farther to the right, and "woolly" opacities in the right middle and lower zones and left upper and middle zones No radiological abnormality of the skeleton.

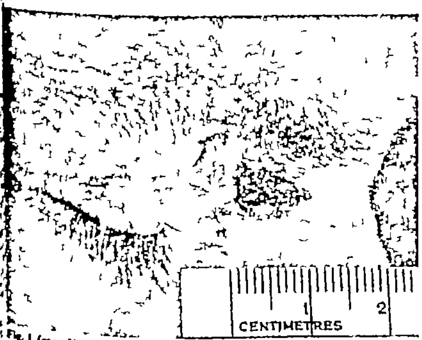

Fig. 1 (case 1)—Ulcerated cryptococcal granuloma of skin (May 1950)

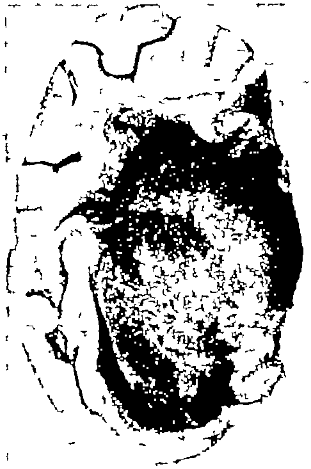

Fig 2 (case 1)—Hæmorrhagic cryptococcal granuloma of brain (gap between the lesion and surrounding tissue is an artefact) (Actual size.)

Treatment

Courses of intramuscular penicillin (500 000 units six hourly total 36 000 000 units) and of sulphadiazine (1·0 g six hourly by mouth, total 50 g) were given over eighteen and twelve days respectively from May 26 On June 8 a course of potassium iodide by mouth was started; the dose was increased from 0·3 g twice daily to 2·0 g three times a day by June 17 at which level it was continued without apparent side-effects until the end of the illness Throughout this stay in hospital the patient had intermittent fever up to 100°F (37·8°C); he had no respiratory symptoms apart from slight cough. His condition did not change and he was discharged on June 18

Progress

On July 21 he had been afebrile since leaving hospital; his skin lesions remained unaltered. On Aug 25 he was back at work and feeling very well although a little breathless on exertion On Oct. 6 he was admitted to hospital elsewhere because of malaise tiredness, and anorexia during the preceding week; the clinical findings were unchanged he had slight fever; a blood-count showed 5 100 000 red cells per c.mm. Hb 12·7 g per 100 ml., and leucocytes 5000 per c.mm His condition improved with rest and he returned home on Oct 16 feeling well but complaining of occasional slight headache for the first time On Oct 20 he had a fit while at work. On Nov 2 he had another fit and until his death in coma at home on Nov 10 major epileptiform convulsions occurred with increasing frequency in spite of treatment with phenobarbitone.

POST MORTEM FINDINGS

Necropsy (Dr W H. J Baker)

The posterior half of the right cerebral hemisphere contained a hæmorrhagic mass (9 × 6 × 5 cm.) which shelled

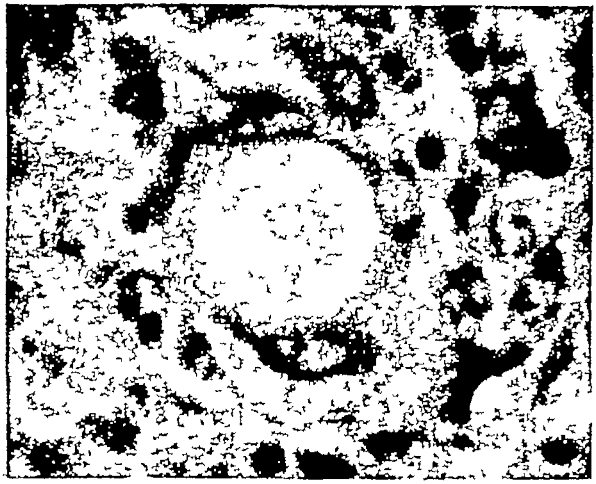

Fig 3 (case 1)—Lymph node biopsy (December, 1947) showing cryptococcus, with typical broad capsule in multinucleated giant cell (Hæmatoxylin and eosin × 950)

out easily (fig 2), the meninges appeared normal There was a small empyema over the lower lobe of the left lung, old adhesions obliterated the rest of the pleural cavities The lungs (each 900 g) showed dense fibrosis of the lower lobes and of the basal and hilar parts of the other lobes, the bronchi were crowded and dilated The upper lobes and the periphery of the lower lobes contained groups of smooth lined cysts (0 1–1 0 cm in diameter) Irregular firm grey nodules (0 2–2 0 cm in diameter) were scattered through the lungs The liver (2020 g) was moderately enlarged, a few white nodules, up to 0 5 cm in diameter, were scattered through it The lymph nodes in the neck, axillæ, and abdomen were firm and moderately large The spleen (500 g) was large, soft, and engorged. The other organs were normal *C neoformans* was isolated in cultures only from the ulcer on the chin, the lungs, spleen, cerebral mass, and C.S F were heavily contaminated with saprophytic bacteria

Histology

All the specimens were fixed in formol saline (4% formaldehyde)

Lymph node biopsy (December, 1947)—Review of the sections showed nothing to support the original diagnosis of Hodgkin's disease the appearances were those of chronic lymphadenitis. No organisms were found in the original sections, examination of 100 new serial sections revealed three typical cryptococci (fig 3)

Cutaneous lesions (fig 4)—The appearances in all three ulcers were identical The ulcerated area was surrounded by hyperkeratotic acanthotic epidermis, there was no evidence of neoplasia The dermis and fascia deep to the margin and base of the ulcer were packed with cryptococci. At first sight most of the organisms appeared to be free in the tissue spaces, under higher magnification traces of histiocytes were seen round many of them. Well preserved foreign body giant cells were numerous at the periphery of the lesions and contained yeasts, singly or in groups. There were a few polymorphs near the ulcerated surface and small clusters of eosinophils and mast cells elsewhere. There was no fibrosis

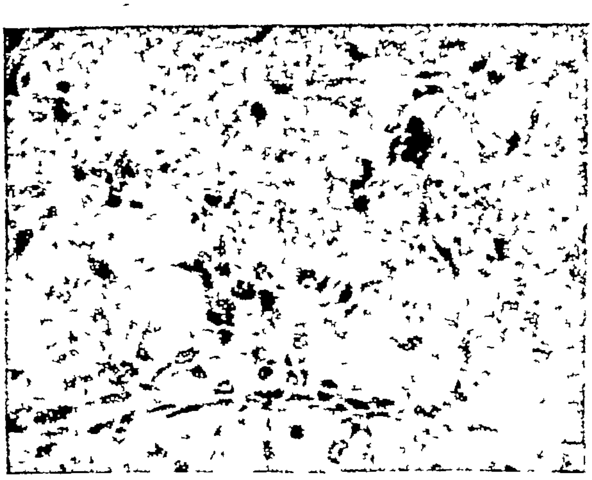

Fig 4 (case 1)—Biopsy of nasal ulcer (May, 1950) showing large numbers of cryptococci in dermis. (Hæmatoxylin and eosin × 400)

Visceral lesions—The pleuræ were fibrotic, no organisms were found in the exudate lining the empyema cavity There was dense hyaline fibrosis of much of the lung tissue, lymphocytic aggregates were numerous in the fibrotic areas, and large, pale, or hyperchromatic cells, some of which resembled the "mirror-image" variety of binucleated reticulum cells were present among the lymphocytes, multinucleated cells and myeloid cells were not found This picture (fig 5) which was seen also in lymph nodes, some portal tracts, and parts of the kidneys, had some resemblance to sclerosing Hodgkin's disease, an occasional cryptococcus was found in the Hodgkinoid tissue, usually in one of the large mononuclear cells The pulmonary cysts were surrounded by hyaline fibrous tissue and lined by simple flat or cubical epithelium, a few of them communicated with the bronchial tree and contained pus Extensive suppurative bronchiectasis and bronchiolectasis were present, gram positive cocci and occasional cryptococci were found in the bronchial exudate and in foci of bronchopneumonia

No evidence of tuberculosis and no acid fast organisms were found in any organ

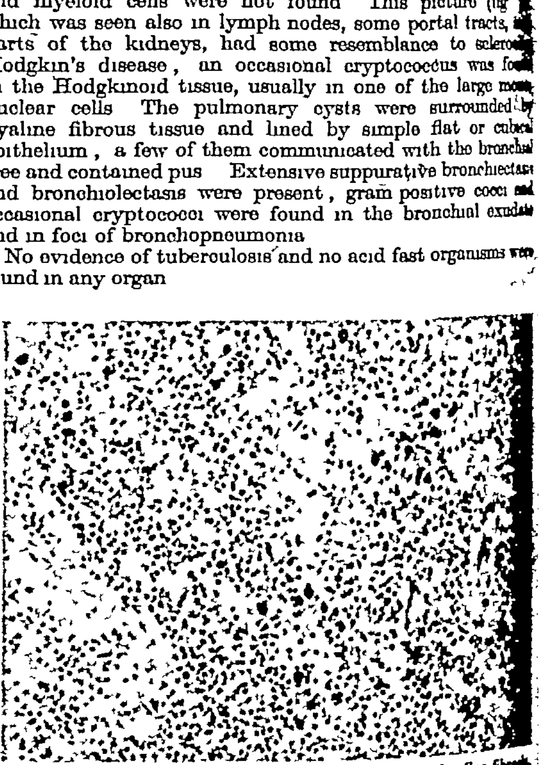

Fig 5 (case 1)—Hodgkinoid tissue (lung), showing hyaline fibrosis, large hyperchromatic cells, and predominance of lymphocytes. (Hæmatoxylin and eosin. × 150)

The nodules in the liver were partly necrotic and consisted of collections of hyperchromatic spindle shaped or polyhedral cells, with larger cells resembling atypical reticulum cells (fig 6), mitotic figures were numerous, no organisms were found in these foci, which had more resemblance to pleomorphic reticulosarcoma than to the Hodgkinoid lesions elsewhere There was an intercellular network of fine argyrophil fibres, least developed where the sarcoma-like tissue infiltrated and destroyed the surrounding tissues. Some cervical, mediastinal, and axillary lymph-nodes contained collections of cryptococci, the appearances being similar to those in the skin lesions, other changes in the nodes ranged from simple reactive hyperplasia and sinus catarrh to sclerosing Hodgkinoid lesions The spleen was engorged The cerebral mass was an accumulation of large pale mononuclear cells similar to those in the Hodgkinoid lesions in the lungs, single cryptococci were found in some of the cells Many vessels in the mass showed recent thrombosis and there was extensive hæmorrhage A narrow zone of brain tissue round the mass was heavily infiltrated by similar cells, the infiltrate extended in the perivascular spaces to the adjacent meninges There was no fibrosis or gliosis

Mycology (Dr H M. Smallwood)

C neoformans was repeatedly isolated from the ulcers and from the sputum and urine Its broad capsule was demonstrated well in nigrosin preparations, budding was observed. It grew well on the common agar media under aerobic cond

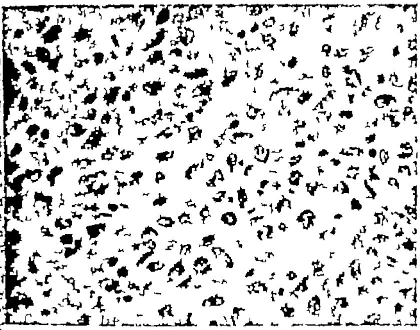

Fig 4 (case 1)—Reticulosarcoma-like tissue (liver) showing several mitotic figures. (Hæmatoxylin and eosin. × 400.)

lous at 37°C and at room temperature. The colonies were mooth and ordinarily white or cream coloured, though old ultures on Sabouraud's maltose-agar medium became tan oloured. No mycelium was produced in cultures kept for p to a year but pseudohyphæ were observed in the peri oneal exudate of experimentally infected mice. Acid, but not as, was formed from glucose, maltose, and saccharose ctose was not fermented. litmus-milk was turned alkaline latin was liquefied in four to six weeks. Intraperitoneal noculation of mice and guineapigs caused a lethal disseminated afection in which the kidneys and brain were conspicuously ffected. The morphological, cultural, and pathogenic haracteristics of the organism identified it as *C neoformans* (Sanfelice) Vuillemin. Sensitivity tests on solid media showed hat it was resistant to penicillin (10 000 units per ml); to strepto mycin, chloramphenicol, and aureomycin (100 µg per ml in ach case); and to sulphathiazole, sulphadiazine, and sulpha midine (10 mg per 100 ml in each case); it was resistant lso to 1 mg of gentian violet per 100 ml, but sensitive to 0 mg per 100 ml.

DISCUSSION

Diagnosis

The diagnosis of torulosis was proved by isolation of he organism. The discovery of morphologically typical rganisms in the lymph node biopsy makes it reasonably ertain that infection with *C neoformans* was of at least hree years standing. The natural duration of torulosis s not known; the duration of most of the published ases was estimated from the time of onset of neurological manifestations, which usually presage death within hree or four months (Cox and Tolhurst 1946). Few ases with longer survival have been reported; the ongest recorded durations are seven years and eight months (case 4 of Reeves et al 1941, Hammack cited by Voyles and Beck 1946) and seven years and three months case 4 of Voyles and Beck 1946); both these patients were still alive, although not cured, when last reported.

Clinically manifest torulosis is not invariably fatal, but he prognosis is almost always bad once evidence of meningo-encephalitis develops. As *C neoformans* has a remarkable affinity for the meninges and brain, torulosis is always potentially very dangerous. Lesions in other parts of the body, however, may heal; published cases of this type reviewed by Gendel et al (1950) were not all mycologically unequivocal, and some were not under observation long enough to justify the presumption of a cure. Unlike other visceral mycoses, torulosis has not yet been shown to occur in a subclinical self-limiting form, but cases in which encapsulated intracerebral collections of cryptococci are an incidental post-mortem finding may be of this nature (Stevenson et al. 1950).

The sources and portals of entry of naturally occurring cryptococcal infection are practically unknown. Carter and Young (1950), who isolated *C neoformans* from a sample of cow's milk in Scotland, found only two previous records of its isolation from outside the animal body—from peaches and from milk.

Several difficulties in diagnosis were illustrated by this case.

Malignant Reticulosis

The patient was long thought to have Hodgkin's disease. As a review of the lymph node biopsy specimen showed nothing more than a chronic lymphadenitis with no resemblance to Hodgkin's disease in support of the original diagnosis, it is remarkable that lesions which resembled those of Hodgkin's disease should have been found post mortem. Cox and Tolhurst (1946) noted that enlarged lymph nodes were recorded in 18% of the cases of torulosis which they reviewed. Though cryptococcal lymphadenitis accounts for the lymph node enlargement in some cases of torulosis, in others tuberculosis (Rappaport and Kaplan 1926), histoplasmosis (Milder et al 1947), sarcoidosis (Gandy 1950), and Hodgkin's disease or some other form of "lymphoblastoma" (Cox and Tolhurst 1946) have been held responsible. Gendel et al. (1950) found that "Hodgkin's disease" had been diagnosed in 14 of the 165 cases of torulosis which they reviewed; in many of the cases the evidence for this diagnosis seems to have been inadequate or was not given in detail. Organisms have not usually been seen in these lesions. Rodger et al. (1951) found that lesions resembling Hodgkin's disease were said to have been present in 3 out of 118 published fatal cases of histoplasmosis, as well as in their own remarkable case of coexistent histoplasmosis, torulosis, tuberculosis, and "Hodgkin's disease." Such observations suggest that certain primary diseases of the lymphoreticular system may predispose to the establishment of mycotic infections, or alternatively that mycotic infections may in some instances evoke proliferative reactions of lymphoreticular tissue which histologically resemble recognised varieties of malignant reticulosis more or less closely.

The evidence in case 1 suggested that the Hodgkinoid tissue was an atypical granulomatous reaction to the fungus infection; cryptococci were found, although with difficulty, in these lesions. Sarcoma-like lesions such as were present in the liver in this case do not seem to have been described before in association with any fungus infection. It is debatable whether they were neoplastic, although their resemblance to pleomorphic reticulosarcomata was close; organisms were not found in them.

Pulmonary Tuberculosis

Although the radiographs had been interpreted as showing pulmonary tuberculosis, no evidence of tuberculosis was found anywhere post mortem. The radiological findings were similar to those which Greening and Menville (1947) described in torulosis. The naked-eye appearances of the lungs were those of cystic disease with fibrosis (cf Cunningham and Parkinson 1950); the fibrosis was associated with Hodgkinoid torulosis, but radiotherapy may have played some part in its development.

Rodent Ulcers

The skin lesions in this case simulated rodent ulcers so closely that the histological demonstration of their non neoplastic nature was completely unexpected. It was therefore interesting to find that a visiting party of American radiologists unanimously suggested torulosis as an alternative diagnosis in this case, and said that in their experience differentiation between carcinoma of the skin and the ulcerative form of cutaneous torulosis can be made with certainty only in the laboratory. Ulcers which are clinically identical with those of torulosis may also develop in histoplasmosis (Rodger et al 1951). Other manifestations of cryptococcal infection of the skin include acneiform and furunculoid lesions; systemic torulosis may be associated also with psoriasiform and other dermatoses from which the organism cannot be isolated (Cox and Tolhurst 1946). Cox and Tolhurst (1946) found that the incidence of cutaneous torulosis in the hundred or so cases which they reviewed was between 4% and 5%.

Skin lesions may be the presenting manifestation of torulosis (Curtis 1950); whether the skin is ever the portal for infection is debatable: as in case 1, the skin lesion observed by Johns and Attaway (1933) developed at the site of a razor-cut, but their suggestion that the fatal meningeal infection was a result of this infection of the skin is not borne out by their account of the patient's history.

Neurological Features

Although necropsy in case 1 revealed a large granulomatous tumour in the right occipital lobe, the patient had first complained of headache only a few weeks before his death. Localising neurological signs were never observed. Daniel et al (1949) indicated that circumscribed cryptococcal granuloma ("toruloma") of the brain is considerably rarer than diffuse cryptococcal meningo-encephalitis. Unlike the "torulomata," which consist of gelatinous masses of cryptococci with little cellular tissue reaction, the circumscribed cerebral lesion in case 1 was a hæmorrhagic mononuclear cell tumour like granuloma in which organisms were scanty.

Treatment

The strain of *C neoformans* which was isolated in case 1 was resistant to various sulphonamides and antibiotics in vitro, and there was no apparent response to treatment with these drugs or with iodide. The inefficacy of treatment of systemic torulosis has been common experience (Mosberg and Arnold 1950), with the possible exception of the sulphadiazine-treated case of Marshall and Teed (1942, 1951). As in case 1, lymphadenopathy accompanying torulosis has been observed to regress after radiotherapy in several cases (Cox and Tolhurst 1946), although with the exception of some cutaneous lesions (Kessel and Holtzwart 1935) irradiation has not been effective against other manifestations of torulosis, and shrinkage of enlarged lymphoid organs is likelier to have resulted from the effect of the irradiation on the lymphoid tissue than from any effect on the organism. Chapman was cited by Stone and Sturdivant (1929) as noting an inhibitory effect of X rays on cultures of the strain of *C neoformans* isolated from their case; their patient, however, did not respond to X-ray therapy. X irradiation had no effect on the strain studied in vitro by Owen (1940).

The Second Patient

CASE-RECORD

A housewife, born in 1925, had good health until December, 1950, when she began to have frontal headaches and pain in the right side of the face; she was 25 weeks pregnant. On March 19, 1951, a submandibular abscess developed on the right side, and was incised because extraction of a tooth did not establish drainage; the incision healed well, but local induration persisted for a few weeks. On March 25 she was delivered of a healthy child, labour and puerperium were normal. On May 16 pain in the left side of the chest was followed by sudden expectoration of about 100 ml of thick brown material. Her temperature was 102°F (38 9°C). Radiography showed a very large abscess in the lower lobe of the left lung and small abscesses in other lobes. Pus from the large lung abscess was sterile; no pathogenic organisms were found in the sputum. Blood: red cells 4,100,000 per c mm, Hb 8 7 g per 100 ml, and leucocytes 8950 per c.mm (neutrophils 85%, eosinophils 2%). Fever subsided during the first days of a week's course of penicillin and streptomycin but rose to its previous level by the end of the week, when a pemphigoid condition of the scalp and painful swelling of one elbow and knee developed. She was admitted to the Thoracic Surgical Centre, Hill Top Hospital, Bromsgrove, on June 6.

Condition on Admission

She was severely emaciated. Her nose was swollen and covered with large hæmorrhagic vesicles, and there were a few similar lesions on the scalp. Suppurative parotitis was present on the right side. The tongue was inflamed and partly covered with small whitish patches. There was an offensive vaginal discharge. The elbows and knees were swollen and very painful. Scattered râles in the right lung were the only other abnormal clinical finding.

Investigations

Blood: red cells 3,500,000 per c mm, Hb 7 5 g per 100 ml, leucocytes 7200 per c.mm (differential count normal). Blood cultures sterile after seven days. Urine: protein +, occasional erythrocytes, leucocytes, and granular and hyaline casts, sterile. Pus from the vagina contained *Trichomonas vaginalis* in large numbers, and culture produced a heavy growth of coliform bacteria and non hæmolytic streptococci. Swabs of lesions on nose and tongue: heavy pure growth of coagulase negative *Staphylococcus aureus*.

Progress

On June 8 a transfusion of 3 pints of blood was given, a course of aureomycin, chloramphenicol, and vitamin complex was started. On June 9 the large pulmonary abscess was drained under local anæsthesia. While being p into position for the operation the patient coughed up pus; cough had not been a feature of her illness, apart the episode on May 16. Little drainage resulted from operation, and there was no appreciable change in her c tion; her temperature still ranged up to 102°F. On J a papular purpuric eruption appeared in the right and within 24 hours covered her body. On June 16 p developed. A heavy pure growth of a yeast was from her sputum, which was now abundant, bloody purulent. Since the organism was presumed to be *C albicans* it was not investigated further; treatment antibiotics was stopped. The patient's condition de steadily, and she died on June 24.

POST MORTEM FINDINGS

Necropsy (Dr C D Cruickshank)

The right pleural cavity was normal; the left pleura cavity was obliterated by organising fibrinous exudate an old fibrous adhesions. The thoracotomy wound opened an "abscess" which occupied most of the lower lobe of th left lung; the thin fibrous wall of the "abscess" was by yellow necrotic material. There was a smaller similar lesion in the upper lobe of the right lung, and another in the middle lobe. The bronchi contained bloody mucopus; no communication was found between them and any of the cavities in the lungs. The liver was moderately enlarged; ill defined firm or purulent yellowish foci, up to 6 cm in diameter, were scattered profusely through it. There was organising fibrinous perisplenitis; the spleen (fig 7) was much enlarged, and its pulp was riddled with focal lesions similar to those in the liver. Similar foci were present in enlarged lymph nodes in the splenic hilus; the lymph-nodes elsewhere appeared normal. Meninges and brain were normal.

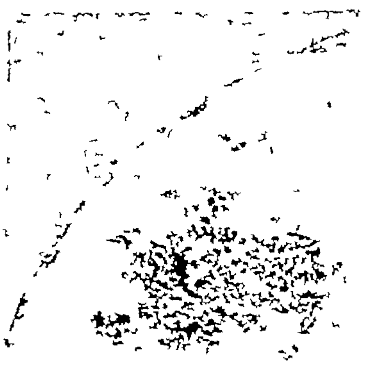

Fig 7 (case 2)—Part of spleen showing confluent abscesses (× 1½)

Histology

The tissues were fixed in formol saline solution.

Appearances of the organisms (fig 8).—The organisms will be described first, because the diagnosis depended on their identification in the sections. They were very numerous in the spleen, lymph nodes, and liver, and were also present in the lungs and bronchi. They were round or ovoid cells 5–10 μ in diameter; their faintly hæmatoxyphil structureless body was outlined by a fine and strongly hæmatoxyphil rim which gave the Feulgen reaction for thymonucleic acid. Further investigation showed that the hæmatoxyphil cell wall was gram positive and coated externally with mucin. The mucin stained metachromatically with toluidine-blue, gave a positive periodic acid Schiff reaction (McManus 1948) and was mucicarminophil; it was not demonstrable after incubation with bull testis hyaluronidase for 24 hours. Although the mucinous capsule was seldom thicker than the cell wall, organisms with the broad mucinous capsule ordinarily characteristic of cryptococci in tissues were found occasionally in all the lesions, particularly in the caseonecrotic pulmonary granulomata and in the bronchial ulcers and exudate. A small proportion of the organisms showed budding.

Viscera.—The lesions which had seemed at necropsy to be lung abscesses showed no microscopical evidence of suppuration but consisted of caseous matter, softening of which had led to cavitation. An incomplete wall of hyaline fibrous tissue intervened between the necrotic material and the adjacent lung, which was fibrotic and infiltrated by lympho-cytes and plasma cells; there were collections of epithelioid histiocytes and multinucleated giant cells at the periphery of the necrotic material The appearances resembled tuberculoma or gumma, but were not typical of either no tubercle bacilli were found but there were occasional yeasts in the tuberculoid tissue Some small infarcts in the lungs showed early organisation the related arterioles were occluded by organising thrombus in which rare yeasts were seen. There was widespread chronic suppurative bronchitis, and some bronchi showed patchy ulceration scanty yeasts were found in tuberculoid tissue in the floor of the ulcers. Yeasts were also present in foci of acute necrotising bronchiolitis and in the narrow zone of pneumonic exudate round them

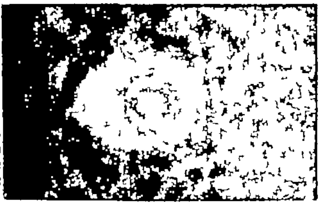
Fig. 8 (case 2)—Typical cryptococcus in pus (spleen) (Hæmatoxylin and eosin. × 900)

The focal lesions in the liver were abscesses; their distribution had no constant relation to the lobular landmarks The earliest lesions showed necrosis of the parenchyma and accumulations of polymorphs yeasts were scanty in them. The larger lesions contained abundant purulent exudate and large numbers of yeasts occasional histiocytes were present but none of them contained organisms and there were no multinucleated forms; the parenchyma and most of the stroma were destroyed and there was no fibrosis. Some lesions involved the walls of tributaries of hepatic veins, and in some instances the abscess had broken through the overlying mural thrombus to discharge into the lumen of the vessel (fig 9) The spleen and some of the lymph nodes, particularly nodes in the splenic hilus were riddled with similar abscesses. The meninges and brain were normal

DISCUSSION

The clinical course and pathological findings in case 2 were unlike those of any case of torulosis in the literature The unusual features make it the more regrettable that the diagnosis of torulosis rests on identification of the organisms only by their appearance in histological sections; the morphological and tinctorial evidence that they were cryptococci, however convincing remains presumptive evidence only. In view of the isolation from the sputum of a yeast which was thought at the time to be *C albicans*, it should be said that the characteristics of the organisms in the tissues were not those of candida

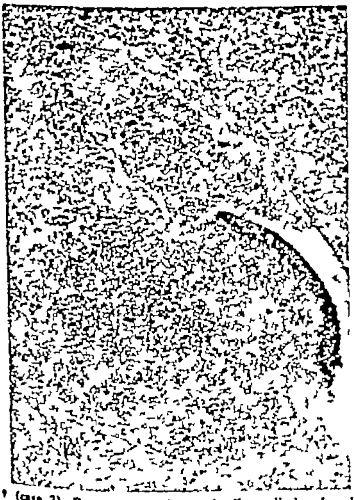
Fig. 9 (case 2)—Cryptococcal abscess in liver discharging into a hepatic vein; dark crescent is thrombus over site of perforation of vessel wall. (Hæmatoxylin and eosin. × 80)

A non-necrotising tuberculoid granulomatous reaction is most characteristic of torulosis and the only common variation is in the amount of the cellular proliferation which is sometimes so inconspicuous that the lesions appear to consist predominantly of great accumulations of cryptococci, among which few tissue cells may be recognisable Caseation is rare (Cox and Tolhurst 1946) and caseous lesions of the large size of those in the lungs in case 2 have not been described. These chronic pulmonary lesions were without doubt the oldest lesions present, and most of the organisms in them were typical cryptococci The true abscesses in the spleen lymph nodes, and liver on the other hand were obviously of very recent development only a small proportion of the great numbers of organisms in them had the characteristic broad mucinous capsule of cryptococci an observation which it is tempting to relate to the poor development of the capsule in young cultures of at least some strains of *C neoformans* (Cox and Tolhurst 1946) Suppuration has been observed only exceptionally in torulosis (Cox and Tolhurst 1946); as it is characteristic of another yeast infection North American blastomycosis (Baker 1942) the latter diagnosis was considered in this case and was excluded because of the structural and tinctorial differences between *Blastomyces dermatitidis* and the organism in question

The distribution of the abscesses suggested reticulo-endothelial phagocytosis of blood-borne organisms as the factor determining the site of these lesions It is possible that cryptococcæmia or cryptococcal septicæmia was a consequence of incision of the pulmonary lesion but, if surgical incision of a cryptococcal lesion could alone precipitate such a fulminating infection as developed in case 2 one might expect to find records of this complication in previous cases, and no similar case has been reported It is conjectural whether treatment with antibiotics played any part in the unusual behaviour of the infection in the terminal phase of this patient's illness though there is some evidence that treatment with antibiotics may predispose to certain mycotic infections and that the presence of certain antibiotics or of impurities associated with them may enhance the growth of some fungi in vitro (*British Medical Journal* 1952) no observations of this kind appear to have been made as yet in relation to cryptococci

The absence of intracranial lesions in case 2 was remarkable in view of the severity of the infection, and was in contrast to the high incidence and overriding importance of meningocerebral infection in the recorded cases of torulosis. The relation between the infection and the lesions observed during life in the skin, mucosæ, and joints is not clear the skin lesions did not correspond to any of those described in association with torulosis. It is impossible to say whether the submandibular abscess was related to the fatal illness, or whether pregnancy or parturition played any ætiological rôle The patient's child was healthy at birth and has remained well Timerman (1930) reported a case of cryptococcal meningo-encephalitis in which cæsarean section was performed post mortem; the baby who died two hours later appeared not to be infected The manifestations of torulosis in infants are said to resemble closely those of toxoplasmosis (Neuhauser and Tucker 1948)

Summary

Two cases of disseminated mycotic infection are described

One case masqueraded as Hodgkin's disease and pulmonary tuberculosis until *Cryptococcus neoformans* was found in lesions which simulated rodent ulcers Cryptococci were found on histological re-examination of lymph-nodes excised when lymphadenopathy first appeared three years earlier Death was due to hæmorrhage in an atypical cryptococcal granuloma of the brain

The second case presented with pulmonary lesions which simulated abscesses but proved to be large caseous granulomata in which morphologically typical cryptococci were present True suppurative lesions, the result of acute terminal dissemination of the infection and containing large numbers of the organisms, were present in the spleen, lymph-nodes, and liver, such lesions have not been described in torulosis previously

I am indebted to Mr B G Scholefield and Dr J F Bromley for permission to publish the clinical history of the first case, to Dr M W Parker for information about the terminal stages of the illness, to Dr A. L P Peeney and Dr H M Smallwood for the mycological findings, and to Dr W H J Baker for placing his post-mortem findings and the viscera at my disposal I also wish to thank Mr R H. F Brain and Dr D J S McIlveen for the clinical summary of the second case, and Dr C D Cruickshank for his report on the necropsy and for the preserved tissues

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A ROCKING-BED FOR POLIOMYELITIS

EDGAR SCHUSTER
O B E, D Sc Oxfd

M FISCHER-WILLIAMS
M R C.P E
REGISTRAR, DEPARTMENT OF NEUROLOGY

From the Electro medical Research Unit (Medical Resea Council), Stoke Mandeville Hospital, Bucks, and the Departm of Neurology, United Oxford Hospitals

ARTIFICIAL respiration by rocking the patient wa advised by F C Eve, who found that the gravitation effect on the abdominal viscera caused considerabl movement of the diaphragm with each swing of th rocking apparatus (Eve 1932, Killick and Eve 193 Wright (1947) introduced a rocking bed in America fo weaning poliomyelitis patients from the respirato This method is in use at specialised centres in the U.S.A and Canada but has not to our knowledge been tri in this country One of us (E S) has designed an constructed two rocking-beds which we have foun useful in the rehabilitation of five poliomyelitis patient in the past year

Patients who require a respirator several month after the acute illness are suitable candidates for th rocking-bed Starting with twenty to thirty minute daily, treatment is quickly increased to several hours Th patient may have to be taught to inhale as the hea of the bed rises and to exhale as it falls Nursing car feeding, and physiotherapy may be given while th bed is in motion, but we have not found this necessar Some patients fall asleep while rocking

ILLUSTRATIVE CASE RECORDS

Case 1—Mrs A, aged 40, developed poliomyelitis o Christmas Eve, 1952 She had severe paralysis of the uppe limbs, the intercostal muscles, and the diaphragm, wit lesser involvement of the legs During the first two month she needed positive pressure respiration whenever th respirator was stopped for nursing care

On admission to Stoke Mandeville Hospital on April 1953, she had been out of the respirator for a maximum o five hours at a time She had flexion contractures of th elbows to 30°, slight cough and sputum, and clinical an radiological signs of collapse of the middle lobe of the righ lung The right dome of the diaphgram was paralysed an high There was little or no movement of the left diaphrag

The usual weaning procedures were supplemented by th use of the rocking bed Within the first week the patient wa spending three hours daily on the rocking bed (fig 1), sh was out of the respirator all day, and slept in it only at nigh and for an hour each afternoon Within six weeks the radio logical opacity of the right middle lobe had cleared and ther was no sputum Three months after the start of the trea

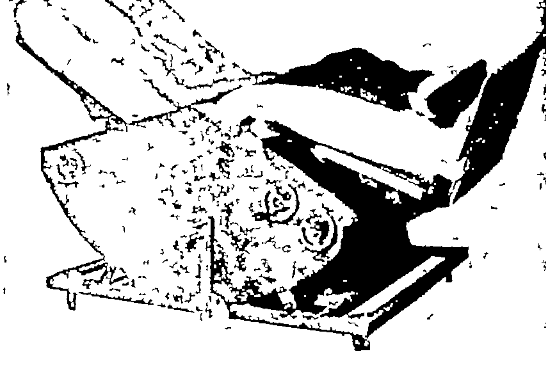

Fig 1—Rocking-bed in use.

ment the excursions of the diaphragm were virtually ormal on both sides Three and a half months after dmission the patient could walk a quarter of a mile, climb tairs, and tolerate a seventy mile car drive She has been weaned to a 'Kifa' cuirass respirator in which she sleeps t night, and was discharged home in November 1953 The ncrease in her vital capacity is shown in fig 2

Case 2.—B C aged 23 developed poliomyelitis on July 13 952. On admission to Stoke Mandeville hospital on Dec 13 952, he was extremely emaciated and had a sacral sore There was no useful movement in the legs and only a little n the arms. He slept in a Drinker respirator and screening n January 1953, revealed very little movement of the intercostals and none of the diaphragm.

Daily treatment on the rocking bed was started A month fter he had hæmaturia and passed urinary gravel This ecurred after a few weeks. Whether this was fortuitous or esulted from the rocking bed treatment is difficult to say enal calculi could not be demonstrated Six months after the tart of treatment both sides of the diaphragm were seen adioscopically to move about 25% of normal The increase n vital capacity is shown in fig 3

The patient was discharged on Aug 15 1953 leading a heel-chair life and sleeping in a kifa cuirass respirator

Case 3.—D.E., a boy aged 10, had acute poliomyelitis in eptember 1950 On admission to Stoke Mandeville hospital November 1952 he slept in a Drinker respirator Treatment on the rocking bed was not started until more than two ears after the acute illness; the increase in vital capacity is shown in fig 2. He now sleeps in a Bragg Paul pulsator nd was discharged home in November 1953

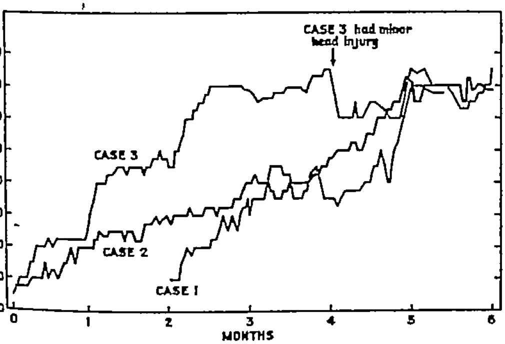

Fig. 2—Vital capacities of three patients during six months treatment on rocking-bed. Time between onset of poliomyelitis and start of rocking-bed treatment was: case 1 four and a half months; case 2, six months; and case 3 twenty-eight months.

DISCUSSION

Since the rocking bed is only one of the means by hich these cases are treated, it is impossible to say xactly what part it plays in their rehabilitation. We hink, however that it not only benefits the lungs and uscles of respiration but also counteracts the ill effects f urinary stasis and improves the circulation and the atient's morale. We have not observed any harm rom this treatment, and regard the rocking bed as a aluable part of equipment

TRUCTURE AND MECHANISM OF THE M.R.C MARK II ROCKING BED

The bed is supported on a rigid stand constructed of ngle-iron bolted and welded at the joints, and carried n four castors. The rocking motion is imparted to a ramework free to oscillate about a centre located as igh as the mechanism permits

The bed top consists of three sections hinged together and f such lengths that the patient's body can be flexed about

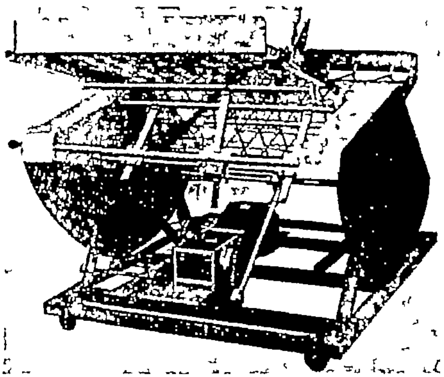

Fig. 3—Rocking-frame.

the hips and about the knees. The three hand wheels shown in fig 1 control the angle of slope of A, the back and head section; B the thigh section and C, the lower leg section. The section A pivots on the frame a few inches from the point at which it is hinged to B The effect of this is that as the head is raised the gluteal region sinks, minimising the displacement of the centre of gravity and the labour involved in turning the hand wheel This important feature of the design was suggested by our colleague Dr F D Stott and contributes to the achievement of our two aims: (1) to keep the centre of gravity as low as possible and (2) to keep the over-all height of the bed small. The object of the first is to allow for smooth and easy rocking and of the second to reduce the strain of lifting the patient on to the bed

A foot-rest is provided which can be moved backwards or forwards and is automatically locked in any position

The rocking frame (fig 3) consists of two inner side members built of aluminium alloy and strip and connected together by distance pieces of Duralumin rod The side members are of the shape of obtuse angled triangles with their base angles truncated, and at the rounded apices of the triangles are housings containing ball bearings. Studs $^{3}/_{4}$ in in diameter fastened from without to the vertical members of the stand with large flanges, form the journals for the bearings, and are the pivots about which the bed rocks Attached to the inner side members are outer members of plywood. The tops of these follow the triangular outline of the inner members, and their lower edges are shaped into circular arcs. A strip of thin metal closes the gap between the upper edges of the inner and outer members on each side Thus the upper part of the stand is completely shut in to prevent any part of the patient, nurse or bedclothes from being caught between a moving and a fixed part

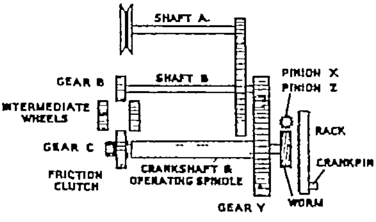

Fig 4—Mechanism.

The bed is rocked with a rotating crank and a connecting rod The small end of the latter has for its gudgeon pin one of the distance pieces connecting the inner members of the frame *The crankshaft is driven at about 16 r p m* by a $^1/_4$ H P motor through a V belt and reduction gearing The final pinion, X (fig 4), meshes with a massive steel wheel, Y, carried at what it will be convenient to call the front end of the crankshaft It is machined so as to form a slideway for the combined rack and crank (shown as "rack" in fig 4) The travel of the crank in the slideway is such that at one extreme the crankpin is coaxial with the shaft and thus conveys no motion to the bed but holds it fixed in the horizontal position, at the other extreme the effective length of the crank is about 5 in and an oscillatory motion of rather more than 40° is imparted

The adjustment of the effective length of the crank is brought about in the following manner A central hole drilled through the whole length of the crankshaft houses the operating spindle This can be made to rotate relatively to the crankshaft by connecting it through gearing to the shaft (to be called shaft B) which carries pinion X at its front end. The spindle and shaft B both carry gear wheels which will be called respectively gear C and gear B When there is no connection between the two wheels, the crankshaft and spindle will turn at the same rate If two intermediate wheels connect gears B and C, the spindle will turn faster than the crankshaft and in the same direction If there is one intermediate wheel, the rotation of the spindle will be reversed The vertical lever shown in fig 1 controls the position of a sector plate carrying on the one side one intermediate wheel and on the other side two When the lever is in the central position, where it is held by a catch, the spindle is free, when it is pushed over into one or the other of the side positions, intermediate wheels are brought into mesh and, if the motor is running, the angle of oscillation of the bed will increase or decrease until the maximum or minimum is reached

Rotation of the spindle relative to the crankshaft acts the crank by a mechanism now to be described. The spind carries at its front end a worm of large diameter relative to pitch, thus the angle of its lead is not much more than and it engages comfortably, if not quite correctly, with straight tooth pinion, Z, whose axis is at right angles to th of the crankshaft This pinion also meshes with a ra integral with the crank Thus, when the spindle rota relatively to the crankshaft, the worm causes the pinion rotate, but at a much slower rate, and the pinion in its tu moves the crank in one direction or the other The tra of the crank is limited at its two extreme positions. either of these positions is reached, no jamming or takes place, because the gear on the spindle is held on shaft by spring pressure against a flange, and slips either end point is reached

SUMMARY

The mechanics of a motor driven rocking bed described

Five patients with respiratory muscle paralysis to poliomyelitis were treated on the rocking bed.

Data are provided, including records of vital cap over six months, which suggest that this is a *means of treatment warranting further trial.*

We wish to thank Dr R B Bourdillon, Dr F D Stott, Mrs P C Stott for their advice and coöperation. Dr Ritchie Russell kindly provided access to the patients his care

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Medical Societies

LIVERPOOL MEDICAL INSTITUTION

Management of Paraplegia

A SYMPOSIUM was presented on Nov 5, with Mr J B OLDHAM, the president, in the chair

Mr A SUTCLIFFE KERR paid tribute to the work of Head and Riddoch and to the enthusiasm and determination of Guttman which had led to the establishment of special centres for the care of *traumatic paraplegia* It was vitally important to distinguish at the outset between a complete and an incomplete lesion, for whereas an incomplete lesion was likely to need surgical treatment, with a complete lesion the paraplegia was irrecoverable, and attention must be directed to early reablement the vertebral lesion might be ignored The development of pressure sores was a reflection on the medical and nursing care they could be prevented—but only by unremitting attention Either the patient must be turned two-hourly, night and day, or he must be taught to be "pressure conscious" *and encouraged to sit up in a* wheel chair as soon as the diagnosis of a complete lesion was established (as it could be within a few hours of injury)

Cases of traumatic paraplegia should be transferred, at the earliest possible moment, to a spinal injury centre where they would have the care of specially trained nursing staff and of a properly equipped reablement unit Of 6 cases admitted to Southport within a week of injury, none developed any pressure sores, and urinary complications were slight These patients were fit for discharge home, and ready for some occupation, in from six to twelve months This contrasted with results in patients admitted weeks or months after their injury almost without exception they had had pressure sores, urogenital infections and joint contractures Reconstructive surgery took months or years, and their inpatient treatment might last from eighteen months to three or four years, with an indifferent fin result

Dr MARCK DAMANSKI, discussing nursing and phys reablement, said that pressure sores must be avoided repeatedly changing the patient's position in bed, and night Patients admitted with pressure-sores mig need prolonged nursing in the prone position, and th might lead to hyperextension of the pelvis and hi joints and the later development of contractures Ea mobilisation of the patient prevented this, and did result in further neurological deterioration No inter fixation or back supports were used Physical exerc restored the lost sense of balance and overdeveloped th non-paralysed muscles Walking exercises came and should be preceded by elimination of severe spastic or deformities Lesions higher than D9 were a gr *handicap to walking*

Mr NORMAN GIBBON found the management of the paraplegic bladder an exercise in applied physiolog A cord injury above the sacral segments allowed unc trolled spinal reflex micturition—the "upper neurone bladder" A lesion of the sacral segments the selves left the bladder paralysed, but the urine wa expressible by abdominal straining—and thus he call "the (relatively) lower motor neurone bladder" initial management of the bladder depended on experience of the surgeon and his facilities Co drainage with a fine urethral catheter gave good in hospital, but in front-line conditions, sup cystostomy was safer

Mr J COSBIE ROSS discussed the results of failure achieve satisfactory automatic voiding with a residual urine *The obstruction of the bladder* might be organic, requiring periurethral Spastic obstruction of the external and internal sp was diagnosed largely from the cysto urethrogram. spastic obstruction he had done bilateral p neurectomy in 20 cases, with satisfactory results, p operative cysto urethrograms showed wide opening of previously closed prostatic urethra Stone formation back pressure effects, and urinary infection were all becoming less menacing as a result of modern methods of treatment, and there had been a dramatic improvement in the prognosis for patients with spinal injury

Mr GEOFFREY OSBORNE did not think that splinting operations were indicated when paraplegia was complete but reduction and splintage were of great value in incomplete lesions

Mr R P OSBORNE said that if all patients suffering from paraplegia were admitted to paraplegic centres within a few hours of the injury decubitus ulcers would not develop Meanwhile plastic surgeons had to find ways of healing such ulcers The general condition of the patient must be made as good as possible his hæmoglobin level must be raised by means of a high protein intake, and local infection reduced by frequent dressings carried out in a treatment room with full aseptic ritual This routine, without the aid of local antibiotics (which were usually useless), resulted in healthy granulation tissue on which patch autogenous split thickness skin grafts were applied Once these had coalesced massage was given daily to all surrounding tissue to reduce the induration As soon as possible carefully planned local flaps of skin and fat were transposed or rotated to replace the skin grafted area and so provide a sound cover By this time the patient was as "sore-conscious" as the surgeons and nursing staff and took care never to sit or lie still except for short periods.

Mr KERR, in replying, discussed the control of flexor spasms by mephenesin peripheral nerve section and tenotomy alcohol block in the lumbar theca and anterior rhizotomy by laminectomy Sexual activity was not necessarily completely lost Special provision must be made for the patient's well being when he went home He needed a special bed and bedding special toilet facilities, doors which allowed access for wheel chairs and ground floor accommodation. Above all he should be encouraged to undertake a regular gainful occupation, preferably outside the home The general practitioner could do much to maintain the morale of these patients and could watch for the earliest signs of complications He could also treat successfully a minor flare up of urinary infection but if the patient had to stay in bed for any reason the closest watch must be kept on old healed pressure sores If these broke down, or if urinary infection got out of hand the patient should be returned to his parent special unit as soon as possible and he should in any case return at intervals for routine checks on his progress

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New Inventions

AN ADJUSTABLE HEAD CLAMP FOR THE OPERATING TABLE

DURING operations on the jaws the patient's head may be steadied by the hands of anæsthetists or nurses, by special pillows or sandbags or by a mechanical head-clamp For twenty years I have used a head-clamp and found it valuable, but it has had limitations, which I have now tried to overcome in devising the simpler model here described.

The base (fig 1) consists of a steel plate readily attachable to the end of the operating table by two stout C-clamps with easily turned hand-screws On this is attached a 'Hydraclamp' hydraulic universal joint, to the arm of which are fixed adjustable callipers which hold firm the patient's head Once the patient's head is fixed in the callipers there is only one mechanism to operate to position the head—i.e the locking wheel of the hydraclamp

There is no difficulty in towelling up (fig 2), because the callipers can be swung out of the way when the towels and mackintosh are placed under the head The callipers are next swung into position and tightened and the edges of the towel are brought up over the patient's upper face and head and over the callipers. Any anæsthetic apparatus may be attached to the clamp Should it be necessary to alter the head position the anæsthetist or a nurse can unscrew the hydraclamp the surgeon can alter the position of the patient's head and the screw can be locked tight once more

The clamp may be left attached to the table for successive cases: it is only necessary to undo the calliper and to raise and swing it away from the patient

It is advisable to cushion the pads with 'Sorbo rubber—$^1/_4$ in. thick for the vertical pad and $^3/_4$ in. thick for the temporo parietal ones.

The calliper arms are not adjustable for length, because they conveniently fit any adult head To use the clamp on a child it may be necessary to build up the vertical pad more thickly Two different heights from the table are available by rotating the calliper section.

This head-clamp ensures rigidity and avoids the fatigue of steadying by hand. Its robust construction will withstand the ministrations of theatre staff

Any inquiries about it should refer to the Oxford head clamp and be addressed to Mr W J Phillips, Loach Electrical Co., 17 Old High Street, Headington, Oxford

Churchill Hospital,
Headington, Oxford

D S HAYTON WILLIAMS
M.A. Oxfd, M.R.C.S. L.D.S. R.C.S.

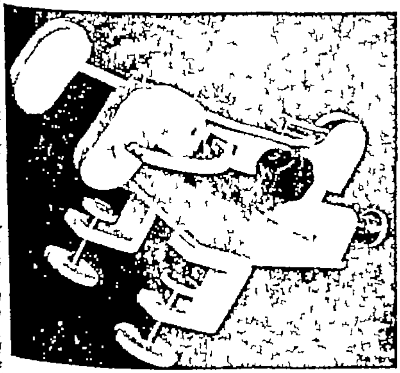

Fig 1—The head-clamp.

Fig. 2—Towelling-up.

Reviews of Books

Clinical Genetics

Editor ARNOLD SORSBY London Butterworth 1953 Pp 580 90*s*

Professor Sorsby's intention in editing this volume was to produce a book to which the medical practitioner could refer for an up-to-date account of the part played by inheritance in any particular condition in which he was interested In the clinical section—three-quarters of the book—he has assigned one bodily system to each of his contributors These come mostly from the United States, Great Britain, and the Scandinavian countries He has taken considerable pains in allocating space to balance the medical importance of any particular system with what is known of its genetics if genetic information alone had been the criterion, diseases of the eye, the skin, and the nervous system would have occupied half the book But since there are already good books on the genetics of the eye and the skin the authors of these sections are better able to give succinct accounts of the more important disorders, and refer the reader to larger works Other contributors, allowed more space, give much more detailed accounts of the evidence on which current opinion about the inheritance of individual disorders is based Unfortunately there is not yet an experienced geneticist working in every field of clinical medicine, and one or two experts, for one reason or another, have not been able to contribute to this book One or two sections have therefore had to be written by a physician better informed clinically than genetically or by a geneticist more familiar with other specialties These authors have been by no means unsuccessful, but clinical or genetic experts will probably be able to detect occasional errors in the descriptions of particular conditions One such instance is the account of cystinuria, where the two main clinical types (clearly differentiated by paper chromatography and by genetic studies) are not distinguished Most sections, however—for example those on physique, ophthalmology, psychiatry, neurology and cancer—are written with a sure hand The illustrations are very good indeed The theoretical section will be of less immediate value to the practising doctor, but much of it makes fascinating reading Professor Neel's account of the progress that has already been made in the study of the symptom-free "carrier" will be a revelation to many readers It is much to be hoped that the book can be kept up to date by new editions

Emotional Factors in Skin Disease

ERIC WITTKOWER, M D , BRIAN RUSSELL, M.D London Cassell 1953 Pp 214 32*s* 6*d*

THIS well-written book should interest even those who do not agree with the authors' conclusions It begins with a general discussion of the psychosomatic approach to dermatology The anatomy and physiology of the skin are then described in an effort to show how emotional factors can produce sensations and objective changes in the skin , and perhaps more is made of the hypothetical functions of the dendritic cells than facts permit In the second part of the book the results of psychiatric investigation in many specific disorders of the skin are described Dermatitis artefacta, malingering, and occupational dermatitis deserve more attention than they receive here, and it would be interesting to know more about the emotional difficulties of patients with manifestly organic disorders—such as unsightly nævi or long-standing lupus vulgaris—or of patients with some dermatoses (e g , dermatitis herpetiformis) which, though incurable, are satisfactorily suppressed by treatment But it is an enjoyable book

Ciba Foundation Colloquia on Endocrinology

Vol 7 *Synthesis and metabolism of adrenocortical steroids* Editors W KLYNE, M.A , PH.D , G E W WOLSTENHOLME, O B.E , M.A., M.B , MARGARET P CAMERON, M.A , A B L.S London J & A. Churchill 1953 Pp 298 30*s*

THE development of knowledge of the hormones of the adrenal cortex has resulted in a mass of facts, hypotheses, and speculation of a complexity to which it would be difficult to find a parallel The Ciba Foundation, in the pursuit of its beneficent aims, brought together many of the leaders of laboratory work in this field in the summer of 1952 The colloquia were wisely managed and led to a free interchange of ideas in the discussion , and these, while remaining lively and colloquial, have been wisely edited Half the present book deals with chemical problems of synthesis, and half with the biochemical problems of formation in the body and of metabolism A speculative and unsure bridge between the two is provided, perhaps, by a paper on the transformation of steroids by X rays, an agent which sometimes mimics vital metabolism The colloquists will welcome these memoranda of their meeting , and specialists in the field will find both useful summaries of work published in scattered papers and inspiration for trains of thought The general reader on the other hand will find most of this difficult and heavy going He may, however, conclude that the chemical part gives no ground for expectation of cheap cortisone, and the biochemical part no theoretical basis for the empirical successes (and disappointments) in clinical practice

Experimental Atherosclerosis

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FOR more than a decade the ætiology of atherosclerosis has been the major research project in the cardiovascular department of the Michael Reese Hospital More people die as the result of circulatory disease than from any other cause—a very large proportion of them from atheromatous plaques in their coronary or cerebral arteries. But the idea that atheroma is an inevitable accompaniment of advancing years has discouraged many would-be investigators in this field Dr Katz points out that arteriosclerosis, not atherosclerosis, is the ageing process of the arteries and with a large group of workers has been trying to discover why some people develop significant atheromatous disease

The title of the book is somewhat misleading and likely to dissuade clinicians from investigating its contents This is unfortunate because the first 120 pages contain an interesting survey of atherosclerosis in different races and in various diseases There is also a well-documented account, with numerous references, of the relationship of human atheroma to plasma cholesterol levels, cholesterol phospholipid ratios, and the concentrations of the lipoprotein fractions separated by Gofman's technique The second part of the book is a review of the studies performed in Dr Katz's laboratories on experimental atheroma in chicks, its relationship to the cholesterol content of the diet, and the ways in which it may be modified by hormonal and other means The results are compared to those obtained by other groups investigating atheroma production in the dog, rabbit, and rat

It is perhaps a reflection of current American therapy that the authors are at great pains to show that lipotropic factors are of no value in the prevention of atheroma. They fully appreciate the uncertainty of translating the results of animal studies in this field to human pathology, and to English readers it may appear that a remarkable amount of time, labour, and money has been spent in investigating a subject of doubtful practical significance.

The Medical Annual (Bristol John Wright 1953 Pp 532 27*s* 6*d*)—A few weeks ago the death of Prof. A. Rendle Short broke the editorial partnership with Sir Henry Tidy which had enhanced the annual's place as a respected friend to doctors all over the world Professor Rendle Short had been joint editor since 1919 This new edition, the last with which he was associated, is the seventy first in the annual's history For a relatively small sum each year, regular readers can keep themselves in touch with much of medical progress This year nearly 50 contributors have combined to provide this welcome service , and the editors have seen to it that no important news has been overlooked For Coronation year, Prof Charles Singer has written an article on medicine in the reign of Elizabeth I, and the book opens with this.

THE LANCET

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Prognosis of Hypertension

FURTHER outlook unsettled! This familiar phrase still summarises our knowledge of the future of the average patient with essential hypertension. We know these days that the stout old lady with her cherished but symptomless "blood pressure" will almost certainly last as long as her contemporaries, and that on the other hand the young man with albuminuria and papillœdema has probably only a few months to live. But the prognosis for the majority of patients who fall between these extremes, is less easily assessed.

This problem has become especially important since the introduction of powerful medical and surgical means of lowering the blood pressure. Hexamethonium, despite some drawbacks, is an undeniably effective hypotensive agent; and as regards surgery, while sympathectomy has fallen somewhat out of favour, subtotal and total adrenalectomy now claim our serious attention. Such therapy is not to be undertaken lightly. Hexamethonium injections are troublesome and unpleasant side-effects are common; operation is risky and the results are not certain. Thus the selection of patients for such treatment is no easy task. Merely to relieve symptoms is an insufficient aim. In uncomplicated cases the symptoms are often due to anxiety about the blood pressure[1] and even when this is not so, the symptoms can usually be much relieved by simpler methods. Without doubt the primary object of administering hexamethonium or of operating must be to prolong life and health; and until we know a good deal more about the natural history of the disease we shall continue to have difficulty in choosing patients for this treatment and in judging its success. Nevertheless certain broad trends are becoming clear. PALMER and MUENCH[2] have lately published a careful follow up of 453 cases, each observed for at least ten years. The patients were originally classified in four grades: grade I, with very slight or no organic change in the heart, kidneys, or brain detectable by ordinary clinical examination; grade II with definite or pronounced change but with no functional impairment; grade III with functional impairment; and grade IV with papillœdema as well. All the patients were simply treated on conventional lines and none had any specific therapy. After ten or more years 64% of grade I, 42% of grade II, 11% of grade III, and 4% of grade IV were known to be alive. From these and other data PALMER and MUENCH draw some general conclusions about the course of hypertension. The relative risk of death is greatest in young persons and decreases rapidly with age. Women live longer than men, and in them the disease seems to run a milder and longer course; elderly women with mild hypertension seem no more likely to die than their contemporaries with normal pressures. Duration of the disease, making allowance for simultaneous ageing, seems to have little effect on mortality. There is a tendency for average age to increase from grade I to grade III, which seems to indicate that patients tend to deteriorate gradually from one grade to the next; but a considerable proportion of patients remained throughout in their original grade.

These conclusions are more or less what might have been expected, though it is perhaps rather surprising to find so little relation between mortality and duration of disease. The conclusions seem to confirm LEISHMAN's[3] suggestion that there are two forms of non malignant essential hypertension. In the "benign" form the disease progresses, if at all, very slowly. In the "accelerated" form the march of events is relatively rapid, though of course nothing like the *Blitzkrieg* of the malignant phase of hypertension. The disease seems to assume one or other of these forms from the very beginning, and only rarely does "benign" hypertension become "accelerated"—as rarely, perhaps, as does a non malignant case become malignant. Nevertheless, these occasional metamorphoses support the view that we are in fact dealing with one disease—essential hypertension—and not with two, or three diseases, as some have suggested. LEISHMAN's subdivision follows logically from previous observations that in general, prognosis depends not so much on the actual height of the blood pressure as on the rate at which it is rising.[4] If the rate of rise has been very slow, very high pressures may be well tolerated and the outlook be favourable. Obviously, however, such a situation can exist only in elderly patients. A very high pressure in a younger person must mean that the rate of rise has been relatively rapid and therefore that the prognosis is not so good. LEISHMAN believes that when in a young or middle aged patient at rest a diastolic pressure of about 130 mm Hg is reached the advance of the disease is hastened.

Before deciding for or against giving hexamethonium or operating it is manifestly important to decide whether the patient has the "benign" or the "accelerated" form of hypertension. LEISHMAN gives some valuable guidance, but judgment may still be difficult, particularly in the case of a youngish man with a moderately raised pressure who as yet shows no evidence of serious damage to the vital organs. It is tempting to treat such people actively, on the sound principle that prevention is better than cure; but then many whose hypertension is "benign" will be subjected unnecessarily to the risk and discomfort of operation or of courses of drug taking; many of the unduly favourable reports on sympathectomy have undoubtedly been derived from series that included cases of this type. The wiser course at present is to observe the patient for some time and to note the rate of rise, if any, of his blood pressure—though admittedly the maximum rate of rise that can be viewed without apprehension is still not clearly established, and also the danger of inducing anxiety by frequent use of the sphygmomanometer must be borne in mind. When cardiovascular complications are present, or when there is evidence of definite strain on the heart or kidneys, the question of treatment is more easily settled; for then in all but the elderly, the prognosis is unfavourable This is reflected in the follow-up by PALMER and MUENCH the survival-rate fell from 42% in grade II to 11% in grade III Radical treatment is clearly called for, even though its long-term results in this type of case are unknown Malignant hypertension has so grave a prognosis that such treatment is always urgently indicated It is rather surprising to learn that PALMER and MUENCH found even 2 out of 50 patients in this group alive after ten years, but spontaneous regression takes place occasionally[4]

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[1] Stewart, I McD *Lancet*, 1953 i 1001

[2] Palmer R. S., Muench H *J Amer med Ass* 1953 153 1

[3] Leishman A W D, *Brit med J* 1953 i 1131

[4] McMichael J *Ibid* 1952 i 933

Thus the forecast of untreated hypertension is gradually becoming a little clearer Further clarification would be greatly hastened by an agreed uniform system of grading In some systems the grades are too vaguely defined Others rely over-much on subjective interpretation of clinical data—the system used by PALMER and MUENCH seems open to this criticism SMITHWICK's[5] method of assigning a numerical value to various significant clinical findings, and grading the patient according to the sum of these values, seems sound in principle, though possibly his present classification gives too little weight to the retinal appearances Some such system will probably prove the best, but it may not be easy to reach general agreement on the relative importance of the various findings

The Anæsthetist's Responsibility

THE anæsthetist's responsibilities are steadily growing, and WHITACRE[6] has named three main causes first, the great increase in elective operations on good-risk patients, second, the increase in the number of long and complex operations, the success of which depends to some extent on the anæsthesia, and third, the ever-increasing number of operations on poor-risk patients To these three causes WHITACRE might have added the gain from modern drugs and techniques, including induced hypotension, which aid the surgeon and whose safety and success depend on the anæsthetist's judgment The anæsthetist is clearly responsible for the choice and administration of an anæsthetic, and he may be legally accountable for any resulting injury[7] There are, however, times when immediate responsibility could equally be assumed either by the anæsthetist or by the surgeon

During a major operation the anæsthetist can best assess the patient's state and give intravenous infusions, but not everyone agrees that the decision to initiate such treatment should be his

Acute respiratory infection is a contra-indication to all but essential operations, since it enhances the risk of postoperative pulmonary complications This seldom leads to disagreement, but the prevention and treatment of postoperative pulmonary complications sometimes does Perhaps the most helpful measure is the administration by inhalation of a vasodilator such as isoprenaline, and postural drainage with vibratory and clapping percussion of the chest[8] Should this rest with the anæsthetist or with the surgeon?

MORTON and WYLIE[9] described a series of deaths due to regurgitation or vomiting during anæsthesia, and suggested that this catastrophe, being related to food or fluid in the œsophagus or stomach, was preventable by precautionary measures Preparation for an emergency operation may necessitate the introduction by the anæsthetist of an œsophageal tube, but not all surgeons and obstetricians would like him to undertake this.

During the operation the surgeon wants the patient in the best position for operating; but the anæsthetist may find that this impairs circulatory or respiratory activity The surgeon may claim that a steep Trendelenburg position is essential for the satisfactory performance of, for example, combined asynchronous abdominoperineal resection of rectum, and that his supports would interfere with the operating field or would not hold the patient in a suitable position, while the anæsthetist may say that the only other way of keeping the patient in this position—i e, by shoulder supports—entails the risk of brachial plexus palsy even though the arms are kept by the side

In many hospitals diathermy is used routinely in operations, and there are occasions when the most satisfactory anæsthetic sequence includes an inflammable agent A decision must then be reached as to which of these—the diathermy or the inflammable anæsthetic—is needed most by the patient

In the immediate postoperative period the choice of sedatives and pain-killers must depend somewhat on the anæsthetic technique at the foregoing operation. Who, therefore, should prescribe these drugs?

Surgeons may prefer certain types of anæsthesia and physicians commonly advise against some anæsthetic technique, or in favour of another, for operations complicated by medical disease These opinions are valuable, but should not overrule the choice by the anæsthetist, who is ultimately responsible, and, if suitably trained, is in a better position to select the most suitable technique In a well balanced team these matters are discussed and settled without argument or direction, but if agreement cannot be reached the anæsthetist would be unwise to adopt a technique which in his opinion might be injurious Beyond this, it is often not possible (nor perhaps is it desirable) to make a sharp division between the responsibility of the anæsthetist and that of the surgeon—though the improved training and status of the anæsthetist, and the growing scope of his work are bringing him to the fore The field of each has to be defined only in legal actions or when surgeon and anæsthetist cannot readily work together—and happily for the patient, this situation is rare

Lung Lesions in Arthritis

CHANGES in the lungs are associated much less commonly with rheumatoid arthritis than with some of the other mesenchymal diseases of unknown origin. Where pulmonary lesions have been regarded as a manifestation of the "rheumatoid disease," the radiographic picture has usually been of diffuse reticulation ELLMAN and BALL[11] reported three such cases, 2 of which came to necropsy Histologically the lungs showed interalveolar fibrosis with mononuclear-cell infiltration Similar cases were later described by LEYS and SWIFT[12] and by BLOOM and RUBIN[13] In a study of visceral lesions associated with rheumatoid arthritis, BAGGENSTOSS and ROSENBERG[14] examined the lungs from 30 cases and failed to find any lesions which could in any way be considered specific, though a high prevalence of adhesions suggested that the pleura was commonly involved. Necropsy studies in cases of rheumatic fever have likewise failed to establish "rheumatic pneumonia as a specific entity. In scleroderma diffuse fibrosis is not uncommon, and characteristically produces a reticular pattern in the lower half of the lung fields.[15] In systemic lupus erythematosus RAKOV and TAYLOR[16] and FOLDES[17] have described a chronic interstitial pneumonitis which may lead to collapse of lung and respiratory failure. BAGGENSTOSS[18] confirmed this and described a peculiar basophilic mucinous œdema of the alveolar walls and of the peribronchial and perivascular tissues, associated with the interstitial pneumonitis and with alveolar hæmorrhages. A relation between lung lesions and joint disease is clearly evident in hypertrophic pulmonary osteo-arthropathy. The mechanism of the changes in the bones and joints in this condition remains obscure, though FRIED[19] suggested that "dyspituitarism" is a factor. Where the lung lesion is neoplastic, pain in the joints is often quite severe and with the associated swelling and stiffness may simulate rheumatoid arthritis. The fact that joint symptoms may be the presenting manifestation of a bronchial neoplasm is well known.[20] This sequence arose in each of the 14 cases of acute pulmonary osteo arthropathy collected by RAY and FISHER[21] in a series of 130 cases of carcinoma of the lung.

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[5] Smithwick R H J Amer med Ass 1951 147 1511
[6] Whitacre R J Ibid, 1953 152 1407
[7] See Lancet Oct, 3 1953, p 728
[8] Palmer, K N V Sellick B A. Ibid, 1953 i 164
[9] Morton H J V Wylie W D Anæsthesia 1951 6 190

[10] Helme J M Proc R Soc. Med 1949 42 705
[11] Ellman P Ball R E Brit med J 1948 ii, 816
[12] Leys D G Swift P N Ibid, 1949, i, 434
[13] Bloom J Rubin J H Canad med Ass J 1950, 63, 35
[14] Baggenstoss, A H Rosenberg, E F Arch Path 1943 35,

Much more florid lung lesions than the interstitial pneumonitis occasionally reported hitherto may apparently be associated with rheumatoid arthritis when the patient is exposed to dust inhalation. From a study of coalminers seen by the Cardiff Pneumoconiosis Medical Panel, CAPLAN[22] has discovered a relation between an arthritis of rheumatoid type and the presence of massive shadows in chest radiographs. Of 14 000 claimants for pneumoconiosis disablement benefit, 51 were found to have rheumatoid arthritis. About 90% of these 51 had massive pulmonary fibrosis compared with only 30% of all the men examined. Furthermore in 25% of the arthritics the radiographic opacities in the chest were of a distinctive type often easily distinguished from the usual appearances of progressive massive fibrosis. The characteristic feature was the presence of multiple, well-defined, round opacities 0 5–5 cm. in diameter, distributed throughout both lung fields but particularly common at the periphery. In cases with this type of lesion the background of simple pneumoconiosis was commonly slight or absent. The opacities seemed to develop rapidly, within months, and thereafter to remain stationary in the majority of cases. The remainder of the arthritics showed either typical massive fibrosis (with opacities which were less well defined, more irregular in outline, larger, rarely more than two in number, and commonest in the right upper zone), a mixture of typical fibrosis and 'round' lesions, opacities indistinguishable from unmodified tuberculosis, or (in 4 cases only) simple pneumoconiosis alone. The severity of the joint lesions was unrelated to the extent and character of the lung changes. Constitutional symptoms were notably absent, even when tuberculosis was suspected, and respiratory function was usually not greatly impaired.

CAPLAN points out that in order to discover whether a relation exists between dust inhalation and rheumatoid arthritis it would be necessary to compare the incidence of rheumatoid arthritis in non miners with that in miners without pneumoconiosis, with simple pneumoconiosis, and with massive pneumoconiosis. In another coalfield the prevalence of rheumatoid arthritis was reported to be higher in non miners than in miners.[23] The true nature of the lung lesion encountered in CAPLAN's cases cannot be established until the difficult task of obtaining material for histological examination from an early case is accomplished. In 3 fatal cases the lesions were composed of fibrous tissue; tubercle bacilli were identified in each of these. CAPLAN suggests tentatively that the lesions are probably allied to tuberculomata and are a form of tuberculosis modified by dust. He believes that the joint changes may be a manifestation of "tuberculous rheumatism." The existence of "tuberculous rheumatism" as a true entity has been debated at intervals ever since PONCET suggested the possibility in 1897, but in the absence of clear diagnostic criteria the majority of clinicians probably remain sceptical. Whether or not CAPLAN's observations can be regarded as providing new support for this concept, he has clearly uncovered an intriguing and hitherto unrecognised syndrome, and clinicians will be on the watch for this in other areas where the hazard of dust inhalation is encountered.

Annotations

SMOG MASKS

LAST week the Minister of Health announced in the House of Commons that doctors could prescribe under the National Health Service "smog masks" for patients with cardiac or respiratory disease. The Ministry has developed two very simple designs: one is like an ordinary surgical mask and the other a cotton tissue pad held over nose and mouth by a soft metal frame. The surgical mask has the less resistance to breathing but unfiltered air can enter quite easily at the sides. The frame mask if carefully shaped to the face is much more efficient; but it is also more of a respiratory obstruction. For the healthy person each is no more than a somewhat tiresome encumbrance; for the dyspnœic patient, however, even the slight respiratory resistance may be unpleasant, particularly with nose breathing in the frame mask. Some people will find a woollen scarf over nose and mouth a more convenient arrangement: the Ministry has itself remarked that this would probably be as effective as the surgical mask.

A number of practical questions arise. When should the mask be put on? Should one wait till early symptoms appear or instruct the patient to protect himself as soon as the atmosphere thickens? Need people on the fringes of a polluted area bother with masks? Where should one strike the balance between avoiding respiratory resistance and providing protection? These questions can be answered only by experience. But it must be remembered that (as the Ministry has already pointed out) such masks cannot provide complete protection, and also that polluted fog only becomes really dangerous when it is very cold.[24] One might suggest, therefore, that if the weather is cold (approaching freezing point) a bronchitic should be advised always to wear a mask whenever a fog develops to which he must expose himself, but that under warmer conditions he need wear a mask only if the fog is exceptionally thick and dirty, or if he begins to feel a need for some protection There seems no point in sentencing people to be mask-bound unnecessarily It would be sensible if the patient could work out in advance how to make least disagreeable whatever device suits him best—for instance, by adjusting the tapes or (if necessary) the filter-pad or by obtaining a scarf of comfortable thickness Other less dramatic measures should not be forgotten verifying that both bedroom and living room can be kept warm in cold weather, seeing that fog shall be excluded as far as possible, and arranging, if possible, that the patient can stay at home whenever a severe fog occurs

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[15] Shuford, W H., Seaman W B Goldman, A *Arch. intern. Med.* 1953 92 85

[16] Rakov H L, Taylor J S *Ibid* 1942 70 88

[17] Foldes J *Amer J clin Path* 1946 16 160

[18] Baggenstoss, A H *Proc. Mayo Clin* 1952 27 412

[19] Fried, B M *Arch. intern Med.* 1943 72, 565

[20] Annotation, *Lancet*, 1944 i 3 8

[21] Ray, L B Fisher H I *Ann intern. Med* 1953 38 230

[22] Caplan A. *Thorax* 1953 8 29

[23] Lawrence, J S Aitken Swan, J *Brit. J industr Med* 1952 9 1

[24] See *Lancet* Nov 7 1953 p 970

The analogy with the cholera epidemics and the *Sanitas Sanitatum* campaign of the last century is provocative The mortality-rate is similar or greater, the ultimate cause is a social one yet the immediate pathogen is not known, and it has needed a really spectacular death-rate to focus attention on conditions which have been lethal on a small scale over decades or perhaps centuries Reflection on the analogy suggests that, today, public-health measures to clean the air are going to be more rapidly effective than experimenting with filters of inhaled air, necessary though these may be in the short term But whether prevention or cure be the more important, the most urgent need for both is to know what the dangerous pollutants are grit, smoke, sulphur compounds, tarry matter, or some specific organic substance or group of substances Such knowledge, telling us what the air should be purged of, could do more than anything else to prosper our twentieth-century campaign for *Claritas Claritatum*

SYNTHETIC PITUITARY HORMONES

UNLIKE the hormones of the anterior lobe of the pituitary, which appear to have specific endocrine target organs, the hormones of the posterior lobe are more general in action Preparations obtainable from the desiccated posterior lobe cause widespread contraction of involuntary muscle—the oxytocic effect—together with a pressor effect due to vasopressin, which is not antagonised by adrenolytic agents

Progress has now justified the naming of two independent principles Professor du Vigneaud and his colleagues at Cornell [1] have not only succeeded in separating the two hormones—oxytocin and vasopressin—but, by bringing the modern armoury of the protein biochemist to bear, they have shown that the striking contrast in physiological action conceals an unexpected similarity in molecular structure Originally considered to be protein macromolecules, oxytocin and vasopressin have now been shown, by selective enzymic attack followed by chromatography of the fragments, to be polypeptides containing 8 amino acid residues with an approximate molecular weight of 1000 Thus, oxytocin consists of five amino acid residues—cystine, tyrosine, isoleucine, glutamic acid, and aspartic acid—arranged in ring form with a tripeptide tail (prolyl leucyl glycyl amide) attached to the cystine residue This molecule has been synthesised and the product is indistinguishable from natural oxytocin in biological, chemical, and physical properties The synthetic hormone possesses full oxytocic potency and is active in man, stimulating labour and inducing the ejection of preformed milk The structure of vasopressin differs from that of oxytocin only in that the leucine and isoleucine residues of the oxytocin molecule are replaced by phenylalanine and lysine respectively The synthetic polypeptide, without final purification, possesses both pressor and antidiuretic activity

As alternative drugs are available, these pituitary hormones have not found very widespread application, and the new syntheses are unlikely to have much immediate effect on clinical medicine Yet the scientific value of this notable achievement can hardly be overrated The first polypeptide hormones have been synthesised, and perhaps the preparation of synthetic corticotrophin (A C T H) is not as far away as we imagine.

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[1] See *Science* 1953 118 543

BACTERIAL RECOMBINATION

THE recombination of bacterial cells was discussed by the International Congress of Microbiology in Rome this autumn, and the subject has also been reviewed by Lederberg and Tatum [1] The transference of hereditary characters from one bacterial cell to another was first proved in vivo by Griffith,[2] who changed pneumococcal types by injecting mixtures of types into mice, and Alloway [3] demonstrated that this change also took place in vitro The factors controlling the exchange of capsular types were determined by Avery and his colleagues[4] While this work was in progress Beadle and Tatum[5] demonstrated, in biochemically deficient mutants of the mould neurospora, a form of sexual exchange, and determined the steps by which these organisms synthesise essential foods Turning to bacteria, Tatum and Lederberg [6] showed that a means of genetic exchange existed between mutant strains of bacteria derived from the stock strain of *Escherichia coli* K12 Recombination of these organisms could be detected, because the mutant strains required different essential metabolites for growth, and thus a medium could be designed so that only cells which had exchanged genetic material with cells from a different mutant strain were able to grow Hayes[7] found that in *E coli* mutants resistant to streptomycin the transference of genetic material was unidirectional, one strain acting as the donor cells and the other as the receptor cells Hayes [8] believed that there is only a limited exchange of genetic material, and that the donor cell need not be intact

Two further types of bacteria have been shown to undergo genetic recombination Alexander and Leidy[9], found that a type transference, similar to that seen in pneumococci, occurred in strains of *Hæmophilus influenzæ*, while Zinder and Lederberg [10] discovered a hitherto unknown means of genetic transfer in strains of *Salmonella typhimurium* Here the genetic transfer was apparently due to bacteriophage action, and this type of recombination has been named transduction

From all the evidence it seems probable that both in *E coli* and in *S. typhi* the genes are arranged linearly along one or more chromosomes, but this has not yet been confirmed by cytological studies. In pneumococci and *H influenzæ*, on the other hand, the transforming agent is desoxyribonucleic acid (D.N.A) derived from the type of organism into which the cells are to be changed This change of type by a chemical compound seems a far cry from the sexual fusion of *E coli*, but apparently the gap may be bridged by observations on *S typhi* Here the genetic exchange is due to transfer of material by a phage, although the type of genetic change is similar to that in *E coli* Hershey and Chase [11] have shown that phage infection is due essentially to the entry of the phage D N A into the bacterial cell, hence there is indirect proof that in *S typhi* the essence of transduction is the transference of D N.A from one cell to another Probably, therefore, in all cases the essential material

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1 Lederberg J Tatum E L *Science* 1953 118, 169
2 Griffith F *J Hyg Camb* 1928 46 1
3 Alloway J L *J exp Med.* 1932 55, 91
4 Avery O T MacLeod, C M MacCarty, M *Ibid* 1944, 79 137
5 Beadle G W Tatum E L *Proc nat Acad. Sci, Wash* 1941 27 499
6 Tatum E L Lederberg J *J Bact* 1947, 53 673
7 Hayes W *Nature Lond* 1952 169 118
8 Hayes W *J gen Microbiol* 1953 8, 72
9 Alexander H, Leidy G *J exp Med* 1951, 93, 345
10 Zinder, N D Lederberg J *J Bact* 1952 64, 679
11 Hershey, A D Chase M. *J gen Physiol* 1952 36 39

exchanged is the same and various types of recombination differ only in the methods whereby D.N.A. is transferred from cell to cell

Bacterial transformations have so far been described in few groups of organisms and even then only in certain strains—which suggests that some special character must be present for transformation to take place This may be the loss of a gene by mutation, in pneumococci and *H influenzæ* it is usually only the rough strains that can acquire a new capsule Unfortunately this is not the whole story since new antigenic types can be produced both in *H influenzæ* and *S typhi* and in bacteria there may be dominant and recessive genes

RHEUMATIC FEVER AFTER MITRAL COMMISSUROTOMY

LESIONS suggestive of active rheumatic carditis are sometimes found in the left auricular appendix of patients submitted to mitral valvotomy; and this suggests that rheumatic carditis may continue in a low grade form for a long time, without overt manifestations of rheumatic fever Soloff et al[1] believe that mitral valvotomy may reactivate carditis, they have often observed a clinical picture after valvotomy which they think may indicate active rheumatic infection This syndrome consists in severe precordial pain and fever, commonly accompanied by arrhythmia, cardiac failure and migratory arthritis and occasionally by psychosis The syndrome developed in 43 (24%) of 179 patients who had been subjected to mitral valvotomy and 3 patients died The onset was usually some weeks after operation and after discharge from hospital In addition 4 other patients developed typical rheumatic fever immediately after operation Aschoff bodies in the papillary muscles and inflammatory cells in the parietal pericardium were noted in a patient who died ten days after valvotomy and in whom left auricular biopsy at operation also showed inflammatory cells In most patients who developed the syndrome auricular biopsy revealed changes suggesting activity but surprisingly in the 3 fatal cases only hypertrophy was found Unfortunately necropsy was done in only 1 case, but this showed evidence of active rheumatic carditis It may be thought that changes in the appendix do not represent the rest of the heart but McKeown[2] has shown that Aschoff bodies in the appendix are usually associated with a similar change in the ventricular muscle.

Soloff and his associates[1] were unable to correlate the post valvotomy syndrome with any recent event of active rheumatism with the operative findings, or with the abnormalities in the auricular biopsy Indeed the proportion of positive biopsies was about the same (40%) in patients who did not develop the syndrome as in those who did. The precordial pain which was a constant feature was always severe and was usually localised to the precordium and left lower parasternal area, and was variously described as vice like tight" or "crushing In some cases it radiated to the back the left shoulder and the epigastrium It was aggravated by movement, respiration change of position and even swallowing but was readily relieved by simple analgesics In many cases the heart increased in size and electrocardiography showed ST and T wave changes compatible with pericarditis or myocarditis in addition to increase in the duration of systole and various arrhythmias. Other investigations proved unhelpful and hormone therapy and salicylates were of doubtful value Whether the pain is attributable as Soloff et al imply to rheumatic pericarditis is debatable Severe chest pain is uncommon in rheumatic fever and other possibilities such as postoperative incisional pain coronary occlusion pulmonary embolism or postoperative pericardial effusion must be considered It seems highly probable, however that the arthritis fever sweating and progressive cardiac failure are manifestations of rheumatic infection Soloff and his associates discuss mechanisms by which the rheumatic activity may possibly be induced Operation might permit spread of endogenous streptococci or increase susceptibility to subclinical streptococcal infections; the incision of inflamed tissue might cause the spread of inflammatory agents or the syndrome might be another example of the hypersusceptibility of the rheumatic subject to non specific stimuli. These workers incline to the view that a patient with rheumatic heart-disease has low grade active carditis throughout his life which is usually maintained in relative quiescence by the natural defence mechanisms of the body

In this series the onset of the syndrome in so high a proportion of patients is disquieting and careful observation of all patients after mitral valvotomy is clearly essential Other workers who have reason to suspect active rheumatism after valvotomy should report their experiences in order that the frequency of this complication may be further estimated Soloff et al say that they approve of giving large amounts of salicylates routinely after valvotomy but such a practice may tend to suppress the general manifestation of the disease, and perhaps mask the nature of the important cardiac complications Whether prophylactic chemotherapy to inhibit streptococcal upper respiratory infection should be given to all patients with rheumatic heart disease, especially after valvotomy is another important question which is still unanswered.

PREPARATIONS OF CORTICOTROPHIN

THE preparation of a pure adrenocorticotrophic hormone from the pituitary was first announced almost simultaneously by Li et al[1] and by Sayers et al[2] Extracts have been assayed principally by two methods which depend on different effects of corticotrophin (A.C.T.H.) on the adrenal cortex of the hypophysectomised animal The first measures an increase in adrenal weight[3] and the second, introduced by Sayers et al.,[4] the disappearance of ascorbic acid from the cortex during the production of cortical hormone Results by the two methods may differ widely and in purifying pituitary extracts Dixon et al[5] have been able to produce separate fractions in which the effect on either adrenal weight or on ascorbic acid depletion predominated Thus there may be two pituitary hormones with adrenocorticotrophic effects though the one affecting adrenal weight might in fact be growth hormone.[6]

The international standard by which the preparations of corticotrophin in clinical use are measured is based on an assay by the Sayers technique where corticotrophin is given intravenously It is now clear that different preparations of the hormone which are of similar potency when given intravenously may have different potencies when given subcutaneously or intramuscularly[7] and in general the available preparations are destroyed more rapidly in the muscles than in the blood stream.

Wolfson[8] discusses three main types of preparation which have been compared: the original crude hormone corticotrophin purified twentyfold or fortyfold by absorption on oxycellulose (Astwood); and a product of the hydrolysis of corticotrophin with a moderately low molecular weight which may be a peptide Of these only the purified preparations retain a high potency

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[1] Soloff L. A., Zatuchni J., Janton O H O Neill T J E Glover R. P *Circulation* 1953 8 481

[2] McKeown, F *Brit. Heart J* 1953 15 433

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[1] Li C. H., Simpson M. E. Evans, H. M. *J biol. Chem.* 1943 149 413

[2] Sayers G., White, A., Long, C. N H *Ibid* p 425

[3] Simpson, M. E., Evans H M., Li C. H. *Endocrinology* 1943, 33 261

[4] Sayers, M A Sayers G., Woodbury L A *Ibid* 1948 42 379

[5] Dixon H B. F., Moore S Stack Dunne M., Young F G *Nature Lond* 1951 168 1044

[6] Stack Dunne, M., Young F G *J Endocrin.* 1951 7 lxvi.

[7] See *Lancet*, Nov 14 1953, p 1031

[8] Wolfson W Q *Arch. intern. Med* 1953 92 108

when given intramuscularly compared with the potency by the intravenous route The preparations produced by hydrolysis, and also the crude corticotrophin with which we are mainly familiar, undergo fairly rapid destruction when given intramuscularly and the rate of destruction varies in different batches and in different individuals Indeed, patients may acquire the ability to inactivate intramuscular corticotrophin while they remain sensitive to that given intravenously Since the hormone is assayed by an intravenous test and is usually given intramuscularly, it is not surprising that the clinical potency of some batches has appeared to disagree with their label

It is likely that, for intramuscular treatment, purified corticotrophin, made up in gelatin so that it is slowly liberated, will turn out to be the most efficient, though Wolfson has noted an unusual complication of peripheral vasodilatation which produced unpleasant symptoms The ordinary complications of corticotrophin therapy —the result of excessive adrenal stimulation—are of course no more easily avoided than with other preparations

THE MUSICIAN'S MOUTH

SOME of the physical signs peculiar to the professional musician have already been described in a fascinating monograph by Francesco Ronchese[1] Examination of the musician's fingers, hands, and mouth may show changes that are characteristic of the instrument he plays In fact, according to Ronchese, it is possible to distinguish between a musician who plays a 'cello or double-bass in a symphony orchestra, and one who performs in a theatre orchestra or dance band The symphony player has a hardening of the skin on the thumb from the so called "thumb-position" which is used only in the execution of "serious" music None of these callosities on the fingers or hand seems to hamper his playing But the acneiform dermatosis which is occasionally seen under the chins of professional violinists may prove a definite handicap, and so may certain abrasions of the buccal mucous membrane in players of wind instruments—a subject lately discussed by Porter[2] Players of reed instruments often have a characteristic mark on the inner surface of the lower lip, where the lip is compressed between the mouthpiece of the instrument and the lower incisor teeth This condition can be sufficiently painful to interfere with playing and is aggravated by irregularities of the teeth Those who play the flute or piccolo are seldom troubled in this way because of the different embouchure they adopt[3] A different embouchure sometimes used by reed instrumentalists may spare the labial mucosa, but only at the expense of the lower incisors, which are often affected by a pressure osteoclasia The saxophone is responsible for more oral lesions than any other reed instrument because of its weight (which may be as much as 16 lb)—a good deal of which is supported by the lower lip Brass instruments, with their extra oral mouthpieces, can produce lesions on the cutaneous surface of the lips,[1] which may actually perforate[4] Although these mucosal injuries are common, there is little evidence to suggest that there is any tendency towards leukoplakia or malignant change

Porter discusses the various ways in which the dental surgeon can help the musician to enjoy greater comfort in playing—methods that are rather more effective than the time-honoured one of covering the lower teeth with a cigarette paper These methods include smooth acrylic caps for the lower incisors and cast metal splints for incisors loosened by bone absorption Full denture prostheses present special problems of their own, and Porter describes the "embouchure denture" intended to be worn only when playing—an appliance first devised by Reichenbach and Brückl[4]

C S F CHANGES IN POLIOMYELITIS

IN poliomyelitis the changes in the cerebrospinal fluid (C S F) usually follow a well defined pattern similar to that in other neurotropic-virus infections Early in the disease, in the meningeal and *early paralytic stage*, there is pleocytosis with both polymorph and lymphocytic cells and some rise in the protein content If the examination is repeated after a week or so, the cells will be fewer and of lymphocytic type, but the protein may still be increasing, indeed, the picture may later be that of *dissociation cyto-albuminologique*, which at one time was thought to be diagnostic of infective polyneuritis Within this broad framework, however, the cellular response may vary widely from case to case and many of those who see much of poliomyelitis will recall an occasional case where the patient almost certainly had poliomyelitis and yet the C.S.F was normal

Bentzon and Hilden[1] have reported their findings in 97 paralytic and 627 non paralytic cases from the 1950 Copenhagen epidemic Their figures show that the higher the total cell count, the greater the percentage of polymorphs is likely to be In children the number of cells is significantly higher than in adults, in neither is there any significant difference in pleocytosis between paralytic and non paralytic cases, but increase in protein is more distinct in the paralytic cases. They also remark that, allowing for the point in the course of the disease at which the C S F was examined, a strikingly large number of cases in their series had a high total cell count—over 1200 per c mm in 19% and over 2400 per c mm in 6% This may be due to the "antigenic" state of the population at risk, but could also conceivably indicate that a variant form of the virus was responsible for the epidemic—a suggestion that has already been made on other, equally tenuous, grounds

AIR IN THE HEART

THE entry of air into the left side of the heart is a dreaded complication of operations involving a left cardiotomy The increasing scope of such operations[2,3] has stimulated research into the cause of death when air enters the left ventricle

Geoghegan and Lam[4] have made a series of observations on dogs Air in amounts varying from 0·25 to 2 0 c cm per kg body-weight was injected rapidly into the common carotid arteries after thoracotomy, and the aortic blood-pressure was recorded by an impedance manometer No impairment of cardiac function or fall in aortic pressure occurred, but signs of neurological damage developed It was concluded that cerebral air-embolism was probably not the cause of sudden death in similar clinical circumstances A further series of experiments was done to determine whether a compressible mass of air in the left ventricle would embarrass the heart in the absence of air in the coronary arterial system In a number of dogs the heart was exposed and a balloon placed in the left ventricle and inflated with air Records of aortic pressure showed little or no change, the left ventricle apparently compensated for the reduction in volume produced by the balloon After removal of the air from the balloon, the same amount of air was injected into the ventricular cavity In a few moments the heart became cyanotic, the aortic pressure fell sharply, and in animals receiving 1 5 c cm of air per kg ventricular fibrillation or asystole and death, rapidly followed rapid aspiration of air

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1 Ronchese F Occupational Marks New York, 1948
2 Porter M M *Brit dent J* 1953 95, 152
3 Porter M M *Ibid*, 1952 93 66
4 Reichenbach E, Brückl H *Dtsch zahnärztl Wschr* 1936, 39 213

1 Bentzon J W Hilden, T *Acta med scand* 1953, 146, 91
2 Bailey C P Bolton, H E Redondo Ramirez, H P *Surg Clin N Amer* 1952 32, 1807
3 Bailey C P Redondo Ramirez H P Larzerle H B *J Amer med Ass* 1952 150 1647
4 Geoghegan T Lam C R *Ann Surg* 1953, 138, 351

from the ventricle was of no value At necropsy most of the coronary tree was seen to contain air In dogs which survived a smaller injection of air the aortic pressure rose as the air passed into the periphery of the coronary arterial system

The mechanism by which air in the coronary arteries produces ischæmia of the heart is of interest. Geoghegan and Lam observed that while the proximal end of a column of air in a coronary artery moved with each ventricular contraction the distal end remained stationary The propulsive force of the column of blood was damped out by air compression, so that the coronary circulation was virtually arrested Since air which had been injected into the left ventricle was collected from the coronary sinus it must have passed through the capillaries

This being so resuscitation might be possible if the air could be propelled rapidly enough through the coronary tree With this in mind the same workers devised a further series of ingenious experiments After the injection of air into the ventricular cavity, the aortic pressure was raised by clamping the aorta distal to the left subclavian artery, thus raising the pressure in the proximal aorta Cardiac massage was then started; and as the air was displaced into the smaller branches of the coronary arteries the main ventricular mass changed from a cyanotic to a bright pink colour and the heart regained its contractile force This produced a second filling of the coronary arteries with air which had been trapped in the ventricular cavity after the initial injection Elevation of the cardiac apex and aspiration of the cavity just before aortic occlusion were found to reduce this refilling By these manœuvres, 17 out of 20 dogs were resuscitated after the injection of amounts of air which would otherwise have been fatal Electrocardiograms of these animals became completely normal, and no residual cerebral damage was found

The entry of air into the coronary arteries is a hazard of all operations on the left side of the heart. It will reassure the surgeon to know that, should this disaster happen, clamping of the aorta vigorous cardiac massage, and aspiration of air from the left ventricle may empty the coronary tree of air quickly enough for the patient to recover completely

CHEMOTHERAPY IN PNEUMONIA

THERE have been few attempts to assess from large numbers of case records, what modern chemotherapy has done for the patient with pneumonia In 1942, during the heyday of the sulphonamides Stable[1] in Pennsylvania, reviewed 15 000 cases and showed that since the introduction of sulphonamides the mortality from pneumonia had fallen from over 30% to less than 10% Now Norris[2] has studied a series of 8000 cases at the Dudley Road Hospital, Birmingham and she has reached some interesting conclusions. Her figures are based on the hospital's diagnostic index and case notes She compared the results of treatment in the years just before the introduction of chemotherapy (1934–38) with those obtained ten years later (1944–48) The mortality from lobar pneumonia she found, was reduced from over 20% to less than 10% but in bronchopneumonia the death rate was almost unaltered The length of stay in hospital was reduced by from four to six days—the exact figure varied with the patient's sex and the type of pneumonia. This represented an annual saving of 2500 bed-days, thus releasing in the one hospital from which these figures were drawn seven beds each year for the treatment of other diseases. The incidence of empyema as a complication of lobar pneumonia was reduced, in the era of chemotherapy from over 4% to less than 1% but the incidence of serous effusions had correspondingly increased Thus, chemotherapy does not prevent the pleural complications of pneumonia but it stops the serous effusion from progressing to an empyema It is good to see what must be a universal clinical impression put on a sound statistical foundation

Norris also compared the effects of sulphonamides and penicillin In male patients she found nothing to choose between them but among women those on sulphonamides apparently did better than those on penicillin It seems on the face of it unlikely that there can be a sex difference in the response of patients to antibiotics, but this may be a point that requires further investigation This confirmation that, in general penicillin may be no better than sulphonamides, which are cheaper and more convenient is also of interest because of the widely held view that the patient who needs to be admitted to hospital for pneumonia does so because he has failed to respond to sulphonamides at home.

The conclusions reached in this inquiry may be faulted by some critics because they have not been obtained by methods which would satisfy the stringent criteria for a controlled therapeutic trial They are none the less of great interest because they are the results of the study of ordinary hospital records and there is a great deal of medical information which must be obtained in this way or not at all

RENAL FUNCTION AFTER UNILATERAL ADRENALECTOMY

ALTHOUGH the adrenal glands owe their name to their position their close proximity to the kidneys has seldom been considered relevant to the important action which they exert on the renal conservation of salt A few reports have indicated that unilateral adrenalectomy may be followed by an increased excretion of salt and water by the kidney on the operated side[1 2] but this has usually been ascribed to incidental damage to the renal nerve supply on that side with release of vasoconstrictor action on the renal vessels, and a consequent increase in filtration rate[3] Simple section of the nerves to one kidney has indeed been followed by an increased excretion of salt by that kidney in comparison with the other kidney[4] and this was shown to be independent of change in glomerular filtration rate so that the change in renal performance was attributed to loss of splanchnic control of tubular activity Although there is good evidence of a nerve-supply to the renal tubule cells[5] the results of splanchnic section might equally well affect the adrenal gland rather than the kidneys themselves

Dempster and Graber[6] now report an interesting series of experiments on dogs, which suggest that removal of one adrenal gland may induce a salt and water diuresis in the kidney on that side, independent of any damage to nerve supply to the kidney or change in filtration rate Urine was collected by catheter directly from the two ureters, and, in control dogs, specific gravity rate of chloride excretion and clearances of creatinine and p-aminohippurate were not much different on the two sides. Such differences as there were bore a relation to the weights of the respective kidneys the ratio of glomerular filtration rate to kidney weight on the two sides was very similar even when the absolute filtration rate was different in the two kidneys When one adrenal had been removed and sodium chloride was infused, the kidney on that side excreted chloride several times more rapidly than its companion without any corresponding deviation in glomerular filtration rate when the weight of the two kidneys was taken into account. This chloruresis was absent in two dogs which were studied

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[1] Stable D C *J Amer med Ass* 1942 118 440
[2] Norris, V *Brit J soc Med.* 1953 7 112

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[1] Cow D *J Physiol* 1914 48 443
[2] Marshall, E. K., Kolls, A C *Amer J Physiol.* 1919 49 302.
[3] Kriss, J P., Futcher P H., Goldman, M L. *Ibid* 1948 154 229
[4] Kaplan S A., Rapoport S *Ibid.* 1951 164 175
[5] Mitchell G A G *Acta anat* 1951 13 1
[6] Dempster W J Graber I G *Acta med scand* 1953 146, 411

days after adrenalectomy, but present in six dogs tudied at 6, 8, 12, 25, 60 and 90 days after the operation. our dogs were subjected to "mock adrenalectomy," n which one adrenal gland was dissected free as for emoval, but then left in its bed; three of these dogs howed chloruresis, the fourth did not. The possibility of ocal spread of material from the adrenal to the kidney was xamined by injecting indian ink into the adrenal gland. he ink diffused into the pelvic fat and lymphatics of the enal capsule, but not actually into the renal parenchyma.

Taken in *conjunction with previous* work, these experinents suggest that direct infiltration of the kidney by drenal steroids may be more significant than the ircuitous path through the greater and lesser circulations hich is the proper route for a hormone; otherwise, it s difficult to see why the opposite intact adrenal did not ontrol the behaviour of both kidneys. The chain of vidence is not quite firm, and the chloruresis after nock adrenalectomy needs explanation, unless it is ssumed that the mere process of dissection damaged he gland. Damage to nerves is admitted, but the latent eriod before chloruresis appeared makes it unlikely hat nerve damage was responsible. Studies on potassiumxcretion in similar circumstances would be worth naking, since a fall in potassium output, concurrently vith the chloruresis, would strengthen the likelihood of n adrenal hormone being responsible. Now that a otent adrenal mineralocorticoid has been detected[7] nd isolated by Reichstein,[8] it might even become ossible to see whether topical application of this subtance would influence renal function. The matter is orth pursuing, quite apart from its general biological nterest, for it may have some relevance to the distant oal of renal transplantation, even although it does not ccount fully for the hyposthenuria of a kidney autoransplanted into the neck.[9]

BACTERIA AT SEA

THE survival in natural waters of bacteria derived rom human excreta has been the subject of inquiry ince the dawn of bacteriology. We know that few of hese survive for long; but in the mechanism of selfurification the relative shares of time, light, oxygen, acteriophage, and other factors, known and unknown, re obscure. The results of investigations are seldom in greement. Even under the strictly controlled conditions f modern experiment it has been found that the "fæcal oli" in water may increase or decrease by 50% after torage in the laboratory for 24 hours[10]; and if this appens in the sterilised bottle it is obviously difficult to orecast what may happen in the stagnant pond or urling brook. For obvious reasons less attention has een paid to the survival of these bacteria in sea-water. he volume of sewage which enters the sea would seem lmost literally a drop in the ocean, and it is easy to be ersuaded that this dilution, together with the summer un and the movement of the tides, robs seabathing of ny perils of infection. Yet the risks may be greater than e realise. Empty a bottle, recork it, and cast it far into our favourite cove in calm weather; if it is not floating here several days later you will probably find it on the trand. The amount of crude sewage which is deposited n the popular beaches of the Lancashire coast is said o be not less than 100 gallons per yard of foreshore per ay[11]; and it is not unknown for a municipal swimmingath to draw its water at high tide from some murky orner of a commercial harbour. It is true that direct vidence of enteric infection acquired while bathing is neagre, but this is not the only way that infection may come from salt water. An epidemic of paratyphoid fever in Germany was traced, not to bathing in the harbour, whose waters were shown to contain the responsible organism, but to eating fish which had been landed and "cleaned" in the harbour.[12] Oysters are supposed traditionally, if erroneously, to prosper best on a diet of diluted sewage, and of their part in spreading enteric infections there is no doubt.[13]

Recently this subject has aroused interest in France. A committee of bacteriologists has confirmed that fæcal organisms as a whole are quickly destroyed in sea water and attribute this to a *pouvoir antibiotique* rather than to bacteriophage.[14] They found that this disinfectant property was absent from boiled sea water and "synthetic sea water" and was increased by oxygenation; it was more apparent in water from the Channel than in that from the Mediterranean. But Buttiaux,[15] who has added much to our knowledge of the bacteriology of water, inoculated several species of salmonella into samples of sea water *obtained* several miles off-shore and found that about half of them survived for 24 hours at room-temperature, whereas in fresh water under identical conditions only 1 in every 1000 survived. *Salmonella typhi* appeared to have the shortest life of the salmonella tested, but apparently only one strain of each species was used. It is a pity, too, that some species of bacterium (or perhaps we should *now* say escherichia[16]) was not used in these experiments; usually this genus and salmonella behave similarly in an inimical environment.

If salmonella does survive for any length of time in sea-water, how important is this? If they last much longer than bacterium we shall have to change our methods of examining the water. But will the careful paterfamilias forbid immersion to his young and keep them digging and sandcastles beside his deck-chair? Not, we hope, in the bicentenary year of Dr Russel of Brighton. If sharks do not deter the Australians, salmonella should not keep us out of the water. *Outbreaks* of enteric infection are not uncommon at seaside resorts and have usually been shown to be due to shellfish, food and drink of dubious quality served by even more dubious hands, or sometimes to the happy go lucky way of living which suits many on holiday. Now that an open-air holiday has become modish, most of those places where tents and caravans gather together enjoy reasonable water supplies and sanitation—thanks to the foresight of the local authorities. It would be a good thing if they all did. It seems, however, that the danger is greater from disposal of sewage by methods *adopted* long before the beaches became as popular as they are today. A pool of sewage dripping from an exposed pipe and washed away (in theory) at every high tide is a poor ornament to any plage. Indeed it is high time that everyone (including some of our largest municipal corporations) realised that to pour untreated sewage into the sea is as *out of date as the* traditional Edinburgh custom of emptying the chamber-pot out of the window—and far more dangerous.

WE regret to record the death of Sir LANCELOT BARRINGTON-WARD, consulting surgeon at Great Ormond Street, and of Mr B C MAYBURY, consulting surgeon to St Thomas's Hospital.

AT the first annual meeting of the College of General Practitioners reported on p 1087, Dr WILLIAM PICKLES was elected to the presidency.

A CHAIR of rheumatology has been established at the University of Manchester with the financial support of the Empire Rheumatism Council. Dr J H. KELLGREN has been appointed its first holder, from Dec. 25.

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7 Tait J F Simpson, S A Grundy H M *Lancet* 1952 i, 122, Simpson S A Tait, J F Bush I E *Ibid* 1952 ii, 226
8 See *Lancet* Sept. 12 1953 p 551
9 Dempster W J *Ann R Coll Surg Engl* 1950 7 275
0 Public Health Laboratory Service Water Sub-committee *J Hyg, Camb* 1952 50 107
1 Lune Fishery Board Report 1945
12 Steiniger F *Z Hyg InfektKr* 1951, 132, 228
13 See *Lancet* July 4 1953 p 40
14 Balsac H H de, Bertozzi, Goudin. *Bull Acad nat Méd* 1952, 136, 514
15 Buttiaux, R. Leurs Th *Ibid*, 1953, 137 433
16 See *Lancet*, Oct. 17, 1953, p 817

Special Articles

COLLEGE OF GENERAL PRACTITIONERS

FIRST ANNUAL MEETING AND FIRST PRESIDENT

THE first annual general meeting of this college held in London in the great hall of B.M A House last Saturday was attended by 400–500 members and associates from all parts of the British Isles and Eire

Dr G F ABERCROMBIE chairman of the foundation council, in moving the adoption of the annual report said that on Nov 10, 1952, when the steering committee was dissolved the ten general practitioner members of that committee had to decide what was to be done next Two courses were open to them (1) to publish the committee's report and wait and see what happened or (2) to found a college at once Believing that if they did nothing then nothing would be done, they resolved to found the college and now, before a year had passed it had been joined by more than 2500 men and women The majority of these were in England, about 300 in Scotland over 100 in Wales and nearly 100 in Northern Ireland substantial contingents came also from Eire Australia, South Africa, and New Zealand and others from widely separated places all over the world A council of the college in Scotland had been set up to deal with Scottish affairs. Telegrams of greeting had just been received from New South Wales and from New Zealand telling of faculties of the college founded there and also one from Canada (from Dr M R Stalker) which said :

"On behalf of the organising committee of the College of General Practice of Canada I wish to extend to you our greetings at this your first Annual Meeting The leadership of your College has been of great assistance to us and we hope to have the Canadian College founded in 1954

The college, Dr Abercrombie said had taken no part in medical politics during the past year and consequently though in contact with many organisations, was in collision with none

After giving an outline of the work of the committees on undergraduate education, on postgraduate education and regional organisation, and on research[1] and of the other activities of the first year Dr Abercrombie ended by saying that the hopes of the founders would be fulfilled only if every member and associate did something for the college. If a request for help from student or practitioner was never to be refused everyone must take a share the steadily increasing burden could not be borne indefinitely on the shoulders of a devoted few The future of the college and with it something of value to the future of British medicine was not in the lap of the gods ; it was in the hands of every member and every associate He announced that the foundation council had presented to the college a Foundation Council Medal to be awarded from time to time by the council of the college for work of the highest merit in the realm of general practice or for services of the greatest distinction to the cause of general practice

In proposing Dr William Pickles of Aysgarth Yorkshire, as first president of the college, Dr J H HUNT hon. secretary of the foundation council said that the foundation council had been conscious from the beginning that it was to a great extent a self-elected body ; and because of this it was hoped that the first president would be someone who had not been a member of this council and who had not been directly connected with the foundation. It was common knowledge that Dr Pickles had done a great deal for British medicine Many practitioners before him including William Budd and James Mackenzie had retired from family doctoring when they became well known But Dr Pickles had absolutely refused to abandon his practice in spite of several temptations throughout the years He would always be admired not only for his original work but also for the unshakeable stand he had made throughout his life for general practice and for general practitioners. Dr F M ROSE (Preston) described Dr Pickles as the doyen of general practitioners in this country his wisdom would be of great service to the college and in honouring him the college would be honouring itself Dr Pickles was then unanimously elected to the presidency

Dr PICKLES said he felt sure that the great general practitioners of the past would have approved of the foundation of this college He was confident that there was no-one present in the hall who did not look upon this as a historic occasion probably one of the most momentous in the whole long history of general practice

The Greek Ambassador M. BASILE MOSTRAS, then handed the president a gift—a gavel made from the wood of an ancient plane tree from the Island of Cos the home of Hippocrates In thanking His Excellency the PRESIDENT said that this gift was a token of the friendship between the two nations and was a reminder of all that Greece had done for the honour no less than for the art and science of medicine It seemed most appropriate that the first treasure of the new college should be a gavel from the birthplace of scientific medicine Dr G I WATSON proposed a vote of thanks which was given with acclamation.

Before the election of the first college council its constitution was discussed

The foundation council it was stated had been particularly anxious that every doctor in the Provinces should feel himself adequately represented, through his regional faculty on the first college council. Dr A BROWN (Cambridge) proposed that the new council should consist of 25 members, but a counter proposal of 20 members was carried by a show of hands. It was agreed that these 20 members should be elected to the council that afternoon As it was desirable that each regional faculty should be represented on the council by at least 1 member of the faculty the council was authorised and requested to make from time to time after consultation with the board of the faculty concerned, such additional appointments as might be necessary to secure or maintain this representation.

In the ballot, out of 37 names put forward the 20 members of the foundation council who had submitted themselves for re-election were re-elected They are :

G F Abercrombie (chairman) F M Rose (vice-chairman) H L Glyn Hughes (hon treasurer) J H Hunt (hon. secretary) G O Barber John Cottrell, D G French Annis Gillie I D Grant, J M Henderson, W V Howells R M S McConaghey J G Ollerenshaw R J F H Pinsent A Talbot Rogers Richard Scott Andrew Smith George Swift G I Watson and J Campbell Young

The first college council thus consists of 4 members from London 3 from Scotland 1 from Wales, 1 from Northern Ireland and 11 from the English counties. To these will be added representatives from all those faculties both at home and overseas which are not already adequately represented

The constitution of the college was reviewed and the by laws were confirmed with two small amendments. It was agreed that a model for the regional faculty boards was necessary ; but the meeting accepted an amendment, proposed by Dr W W FULTON (Glasgow) to allow each faculty scope for development along lines best suited to its local needs

The feeling of the meeting was summed up by Dr ROSE when he said We are here not because we think we are good practitioners but because we want to be better ones.

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[1] See *Lancet*, Oct. 31 1953 p 925

Public Health

Poliomyelitis in Canada

THERE have been nearly 2300 cases of poliomyelitis in Manitoba this year[1]—the second successive year in which there has been a serious epidemic in the province The attack rate of 1 in 330 was unusually high and the proportion of paralytic cases was greater than expected Of all those affected 62 % had paralysis and of those over the age of 20 30 % were paralysed In spite of this the death rate was less than 4 %. 6000 persons were inoculated with gamma globulin : there were 40 cases of poliomyelitis in this group but in 36 of these the illness began within seven days of inoculation Another feature of the epidemic was that there were relatively few cases among children in areas where sanitation was poor

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[1] *Times* Nov 10 1953

The Wider World

THE YUKON TERRITORY

A ROTHWELL
M.A , M B Camb , D C H

EVEN in Canada it is by no means easy to get useful information about the Yukon In the larger towns most people have only heard of the place, and know nothing about it. Indeed, many think that it belongs to the United States and is part of Alaska Workmen who have been there can seldom convey an idea of what it is really like Much of the material to be found in libraries is not up to date, for conditions are changing rapidly

* * *

This part of Canada, roughly triangular in shape, lies entirely to the North of latitude 60° N , which is its boundary with the Province of British Columbia To the West is Alaska, which is part of the United States, and to the East stretch the Northwest Territories of Canada The Yukon itself is a plateau with the watershed of the Ogilvie Range of the Mackenzie Mountains lying roughly transversely to the North of its central portion, and it is crossed by valleys whose bottoms are filled with muskeg from which the rivers drain, and where good fishing is to be had The hillsides are surprisingly well wooded, except where the trees have been destroyed by forest fires or have been cut by loggers for timber or by woodcutters for fuel Scrub poplar, birch, and willow, and several sorts of spruce and pine, are to be found There is so much sunshine during the short summer that many wild flowers grow to amazing size, and excellent raspberries, blueberries, and cranberries abound The woods and scrub are full of small animals, especially squirrels, and big game such as moose and bear may be met

The very pleasant summer lasts from sometime in June until sometime in September , the between-seasons of thaw and freeze may last from four to six weeks each , the rest of the year is winter The winter is cold Snag, in the West of the Yukon, is reputed to be the coldest place in all Canada, with temperatures sometimes 80° below zero Fahrenheit or even lower In many parts of the territory temperatures 60° below zero are not uncommon There is not much snow , the rainfall is slight , so on the whole the climate is dry But there is enough water to fill the rivers that flow into the Yukon—the local Indian word for " Greatest River "

* * *

The country was first travelled by officers of the Hudson's Bay Company who were interested in the fur trade and who established trading posts Owing to the lawlessness prevailing when the mines were being developed during the last decade of the 19th century, the Yukon in 1895 became a district of the Northwest Territories under an inspector of the Northwest Mounted Police The Yukon Act of the Canadian parliament created the separate Territory in 1898, to be administered by a commissioner appointed by the Dominion government itself In effect, the Yukon Territory is a dependency or colony of Canada

Dawson City of Klondike fame, the former capital, is steadily decaying despite considerable seasonal production of gold by the dredgers each summer An increasing number of sightseers are attracted to it by the reputation of the fabulously wicked city of fifty years ago Indeed, Discovery Day, Aug 20, is still the most important bank holiday of the Yukon Territory Whitehorse, the new capital, is now the big town, and more than half of the Yukon's population of 10,000 live there It is the chief town of the Alaska Highway which is doing much to open up a territory of more than 200,000 sq miles f future development A small and inconvenient railw which is fast approaching its maximum carrying capacit connects it with the Alaskan port of Skagway and has a large and growing airport About the centre of t territory is a base metal mining area which is bei actively explored for further ores of value, and whi therefore has a rising population

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For communication with the world outside, this centr area used to rely on stern-wheel paddle steamers plyi the Yukon and its tributaries, and pushing barges befo them during the short season of navigation from la June to early October But this method of carryi traffic was slow, cumbersome, costly in damage and losses, uncertain, and therefore very expensive. Duri the winter one might travel with a dog team and sledg Nowadays aircraft carry more and more of the passenge mail, and goods About three years ago a new road w constructed from Whitehorse to Mayo Landing, abo 350 miles in summer there are powerful ferries at t three big river crossings, and in winter one travels alo a good snow road with well-maintained ice bridges B even this road cannot be used during the four to s weeks of break-up in spring, and the similar period freeze-up in early winter

Prices are still high petrol in Whitehorse costs abo a third more than in Edmonton, and at the more isolate distribution points about double the Edmonton pric Other kinds of goods, including food and spares of a kinds, which " come in " from the outside world are al expensive The local idiom is still to " come in " t and to "go out" from, this area so recently opened t modern travel

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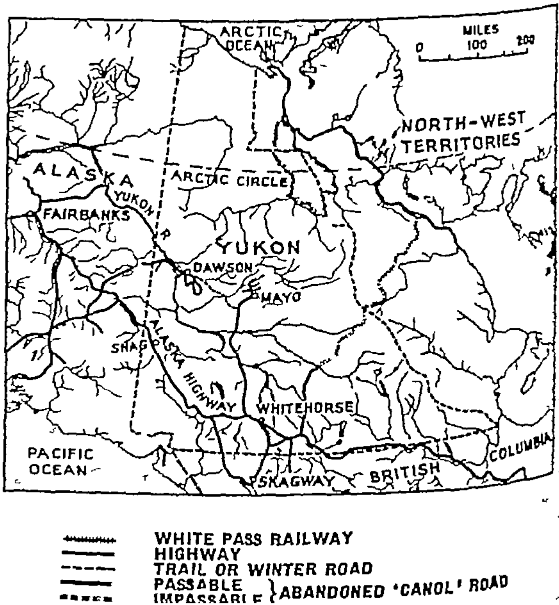
A few old-timers of sterling worth have survived fro the days of the Klondike gold rush that put this part o the world on the map In their old age many of the men are in comfortable circumstances, having sold mini claims of considerable potential value in view of th importance of lead compounds in increasing the efficien of petrol They tell amazing stories of the stirring time of fifty or sixty years ago

There are also many alcoholics Generally they ar younger than the genuine old timers, whom they out number Either the environment is favourable to th development of this disability, or sufferers and potenti



sufferers gather in the land and fail to move out again Other misfits of society are also prominent, such as those who have failed to get on with wife or family, or who have got on too well with somebody else's wife. Many men suffer from lack of success elsewhere or are of plainly inadequate personality They may have exhausted their social benefit, and then have drifted via "skid row" (the place of the down-and-out of Canada) to be hired for some construction or mining task in the North These men work unhappily and incompetently until they lose their jobs or have enough money to go on holiday again They are numerous and their lot is made no easier by the men who supervise them, who are no doubt competent in their own skilled occupations, but who lack the understanding that is necessary to make a success of handling poor human material The quality of this labour the way it is handled, and the effects of the consumption of too much liquor over short periods and long, together make the most difficult problem of the present day The solution is neither apparent nor apparently being sought

On the other hand wages are high and a man may make a "stake" in dollars that will enable him to lay the foundation of success elsewhere. Even the labourer may do this. The skilled workman may more readily succeed because of the lack of skilled men Some of this group have come to the Yukon and discovered a love for the North country that holds them there with the prospect of long enjoyment, and these men will be the excellent old timers of the future

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In the whole of the Yukon three or four doctors practise, and the Services have their own medical staff in Whitehorse and along the Alaska Highway When there was no civilian dentist in the region people might go to Edmonton or Vancouver each about 1700 miles away, for dentures and dental repairs But recently a dentist has come into the Yukon with a large caravan that is his mobile surgery to travel the highway in season Whitehorse has a hospital, and there are small hospitals equipped according to their size and situation in the two other populated places. Thus the way of life of a doctor in the Yukon is indeed general practice, and his results depend in no small degree upon the stuff of which his patients are made There is even some State medicine for the Indians are wards of the Dominion government which pays the doctor a fee for each service on their behalf. These Indians are good patients most of them fully cooperative in their treatment and appreciative of the attention which they receive But history taking may be difficult when the patient is a man of few words and little English.

The officer appointed by the Dominion government to look after the interests of the Indians is the Indian Agent and he is a fine friendly humane welfare worker, doing a job well that is far from easy to do The other social worker for the populace is the Mountie for the Royal Canadian Mounted Police are the successors of the Northwest Mounted Police of the turn of the century Serious crime fortunately is not common From time to time a vehicle may go off the road, an aircraft may become overdue, an old timer living in some remote place may receive a visit and the alcoholic may finally drink himself to death

The pattern of disease is not unlike that in Britain today The exceptions are impetigo which is common and hypertension, which is rare Many elderly men still live in the cabins that they and their partners built many years ago so perhaps the potential hypertensive does not survive in these surroundings, or perhaps the soil lacks the hypertensive factor! Deficiency diseases are rare in the present prosperity for most of the transients are fed by their employers, and the permanent residents know how to look after themselves from long experience One trapper of my acquaintance, a stalwart Yugoslav widower, disappears each October until the following June and lives alone at the end of a distant lake upon the wildlife of the country, with the help of evaporated milk and tea But he takes a thousand tablets of ascorbic acid as part of his regular stores, for even recently the knowledge that the bachelor was more prone to deficiency diseases than the man who was not unaccompanied was associated with the belief that a man could prevent scurvy by taking a squaw

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This Yukon Territory is the Land of Winter where old King Zero reigns supreme for the greater part of the year The dryness and the stillness of the air contrast with the damp cold winter of the British Isles where the weather is much more stormy A log cabin warmed by a wood burning Yukon stove can be very snug Mukluks upon the feet in as many layers of Moose hide as may be needed keep out the cold as efficiently as lined flight boots and are even more comfortable but the skin must be kept dry by well ventilated clothing for sweat freezes readily and leads to frostbite It is a fabulous country, as its own chronicler Robert W Service, has made clear

Medicine and the Law

Spinal Anæsthesia

AFTER a hearing lasting eleven days allegations of negligence in the administration of spinal anæsthetics were dismissed on Nov 12 in a reserved judgment by Mr Justice McNair[1] Two labourers were admitted to the Chesterfield and North Derbyshire Royal Hospital for minor operations six years ago In both cases Nupercaine was injected intrathecally on the same day As a result each of the men had the same symptoms their conditions pursued much the same course and both became permanently paralysed. They sued the Ministry of Health (as trustees of the hospital) and the visiting anæsthetist, alleging negligence or unskilfulness in the administering of the anæsthetic they also sued the company which manufactured the nupercaine alleging that it had negligently permitted a harmful substance or irritant to be present in the anæsthetic or in the ampoule At the close of the plaintiffs' case the manufacturers were dismissed from the action it being agreed that the company was not legally liable. An eminent witness for the plaintiffs had accepted in cross examination a suggestion that nupercaine was as good a spinal anæsthetic as you can get.

The court had to decide if it could between some conflicting medical evidence on the cause of the plaintiffs paraplegia It had to determine the legal responsibility of the Ministry, the anæsthetist and the hospital staff in relation to one another and it had to deal with the plaintiffs contention that the facts spoke for themselves (in the forensic phrase *res ipsa loquitur*) in such a way as to impose upon the defendants the burden of proving that they had not been negligent thus displacing the normal duty of plaintiffs to establish their allegations It must have been an important element in the case that standards of anæsthesia applied in 1947 could not be expected to take account of later theory or research Mr Justice McNair was satisfied that the method of injecting nupercaine by lumbar puncture was widely practised in 1947 before the development of other relaxant drugs No charge of negligence he said was based on the adoption of this method for the two operations in question

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[1] *Times* Nov 13 1953.

The learned judge found himself bound by the rulings n Gold *v* Essex County Council (1942)[2] and Cassidy *v* Ministry of Health (1951),[3] and thus he held that, so far s the anæsthetist was concerned, the hospital's obligation owards the plaintiffs as patients was no higher than the uty (which it had performed) to appoint a competent næsthetist The hospital was not liable in law for his cts of negligence (if any) As for members of the theatre taff, the hospital must assume the vicarious liability of a master for his servants The anæsthetist was a visiting pecialist, comparable to a visiting surgeon or physician or whose acts the hospital would not assume liability The legal maxim *res ipsa loquitur* could not apply where he criticised thing or operation was under the control of wo parties not in law responsible to each other , if what had happened spoke of negligence, it did not speak against ither party individually The evidence had shown, moreover, that, although the anæsthetist was responsible or choosing the anæsthetic, for directing its preparation, nd for generally supervising the activities of members of the theatre staff, he must not be deemed responsible or their casual acts of negligence In consequence, in the udge's view, the normal onus rested on the plaintiffs of proving negligence on the part of the hospital or the næsthetist

What, then, caused the plaintiffs' unfortunate disabilities ? The court remarked that it had been conceded that the injection of nupercaine was not negligent , the medical evidence " clearly established " that the injuries were not caused by an infective organism or by damage to the spinal column produced by the needle The glass ampoules containing the nupercaine had been stored in a 1 in 40 phenol solution, after temporary immersion in a 1 in 20 solution Phenol was the only source of contamination which had been suggested The fact that the same substance was injected by the same anæsthetist on the same day into two patients who suffered the same injuries was something which " seemed to point conclusively to some common factor " The proportion of such injuries after such injections seemed to be 1 in 10,000 The court found it difficult to ascribe to some personal idiosyncrasy on the part of the patient an injury so rare when the common factor was present in the case of these two plaintiffs Glass ampoules could crack , if they did, nupercaine might be replaced by phenol without being noticed In the judge's view, phenol was the most likely common factor , " after the most anxious consideration of the medical evidence " he came to the conclusion that the injuries were caused by the injection of phenol with the nupercaine The phenol could find its way into an ampoule stored in a solution through cracks which the eye could not detect or through molecular flaws in the glass The attention of the profession had been drawn to this risk by Professor Macintosh's book on Lumbar Puncture and Spinal Anæsthesia This book had been published here in 1951 , in 1947 the general run of competent anæsthetists would not have appreciated the risk His Lordship held accordingly that the defendant anæsthetist was not negligent in failing to appreciate it *A fortiori* the theatre staff were not negligent No confident medical opinion could be expressed as to the quantity of phenol necessary to produce the results in question The judge found it difficult to believe that this anæsthetist would have failed to notice a visible crack in an ampoule It had not been shown that the hospital staff had been negligent in handling the ampoules so as to cause invisible cracks As a result of these conclusions the claim must be dismissed both against the hospital and against the anæsthetist

To cite isolated passages from the evidence given by distinguished medical witnesses in a long case is less than satisfactory It may perhaps be mentioned, however, that Prof R R Macintosh, consulting anæsthetist to the United Oxford Hospitals, called by the plaintiffs, stated in cross-examination that he thought their injuries were due to the introduction of phenol into the spinal canal and, asked if there was not a widespread body of opinion that spinal anæsthetics caused these injuries, quite apart from any foreign influence, he replied that he did not hold that view Prof E B C Hughes, professor of neurosurgery in the University of Birmingham, stated that in 1947 an anæsthetist should have known that a normal dose of spinal anæsthetic was dangerous and involved the risk of permanent injury Sir Francis Walshe, F.R.S , consulting physician to University College Hospital, called by the defence, thought that the plaintiffs' paraplegia could not be explained by the introduction of phenol , phenol could not produce such conditions Dr Macdonald Critchley, senior neurologist to King's College Hospital, did not think the injuries were due to phenol , he attributed them directly to the spinal anæsthetic He considered it was high time that the whole problem of the complications of spinal anæsthesia was re examined by the medical profession

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[2] See *Lancet* 1942 ii 127

[3] *Ibid* 1951 i 468

Parliament

Dearer Food

In the concluding stage of the debate on the Address in the House of Commons on Nov 10, Dr EDITH SUMMERSKILL moved an amendment deploring the omission from the Gracious Speech of any reference to the high cost of food " which is bearing so heavily on households with small incomes, and particularly on the old-age pensioners " The Minister of Food had made the astonishing admission that he could not forecast how high prices of food would go under derationing Parliament should be told what controls were to be imposed on food in order that the expensive food, the protein body-building food, should be within reach of the poorest Last winter was the first winter for many years in which old-age pensioners were unable, because of the price, to take up some of the foods which gave them a resistance against colds, coughs, bronchitis, and pneumonia , and at the same time, there was a striking increase in the death-rate

If the Government had no plan for controlling prices, she feared that slowly but surely the pattern of the feeding of the poorest people would come to resemble that of the 1930s which was deficient in meat, bacon, eggs, cheese, and milk The price of all these foods had risen She foresaw that in the home the main wage-earner would be fed, but the adolescents, with their big appetites, would be given a taste of these protein foods and their plates filled up with bread and potatoes, neither of which assisted growth or protected people from disease To ration our available food at a price all could afford, she affirmed, was not a sign of weakness but of that strength of character which was the hallmark of the British people

Major GWILYM LLOYD GEORGE, Minister of Food, declared that food questions could not be dealt with in isolation from other economic problems The greatest service which any Government could give to the community, including those who lived on small incomes, was to strengthen the national economy Two years ago the country was heading for bankruptcy, and all the subsidies and all the rationing in the world could not have prevented disaster without a change of policy A good beginning had been made and the steep rises in the cost of living generally, and in food prices in particular, had been slowed down The reduction of subsidies was a necessary prerequisite for derationing and decontrol which had the overwhelming support of the majority of the people in the country He claimed that the Government's policy of removing restrictions and controls was enabling the public to buy the food they wanted at prices which were becoming more stable than at any time since the war

He did not underestimate the real difficulties of pensioners and people living on small fixed incomes, but the Government last year had raised benefits and pensions rates by 25%. The National Food Survey showed that poorer households and old age pensioners were spending about the same on rationed foods as all other groups Apart from meat and bacon the take-up by old-age pensioners of all other basic foods was about 100%. Their consumption of liquid milk was higher than at any time since 1950 Nearly 33% of national expenditure went on food compared with 30% before the war and 15% went on drink and tobacco against 10% before the war To restore the food subsidies to the level of 1951 would mean subsidies approaching £600 million a year or £500 million more than at present. Where he asked was the money to come from ?

Cleaner Food

The Food and Drugs Amendment Bill, introduced in the House of Lords on Nov 10 extends the powers given under the 1938 Act. The Bill gives the Minister of Food power to require the registration of a wide range of premises, including butchers shops and public houses and the licensing of hawkers and of people who sell food from barrows and stalls. The requirements for registration will be laid down by regulation, and will deal with the construction equipment, and cleanliness of the premises.

The new Bill also provides for the control of the use, in the manufacture of food, of substances which might, if taken over a long period be injurious to health Manufacturers will be required to supply information about the substances they use and regulations can be laid down providing that certain substances shall not be used at all, or shall only be used under a certain strength It will also be possible to control processes which although using otherwise innocuous substances, might injure health The Bill puts on a permanent basis wartime regulations on the labelling and advertising of food and extends them to apply to drugs.

The Ministers of Agriculture and Health are to be given powers to regulate the composition of milk sold under specified descriptions to prohibit the sale of milk from cattle in markets and shows and to require such milk to be stained for identification Port health authorities and food and drug authorities will be empowered to restrict the movement of imported food Other powers will enable the disposal of meat unfit for human consumption to be controlled more effectively

Myxomatosis

In the debate on food and agriculture in the House of Lords on Nov 11, Lord RENNELL deprecated the Ministry of Agriculture s efforts to control the outbreak of myxomatosis in south-east Kent. Was it reasonable, he asked, to protect rabbits against a disease that was going to kill them when we were suffering from their depredations on wheat alone to the extent of nearly £5 million worth of valuable food ? If it was not humane to kill rabbits by a disease was it not also equally inhumane to kill rats with phosphorus ? So far as he knew this disease had infected no other animal of any sort in Australia, whether wild or domestic. Why should we spend our money to make British farming safe for rabbits ?

In his reply Lord CARRINGTON suggested that Lord Rennell s arguments, though they sounded forceful were over-simplified Lord Rennell argued that myxomatosis killed rabbits ; rabbits were a pest therefore myxomatosis must be a good thing But there were other considerations to be taken into account before we decided what to do about this disease It was by no means certain that it would be an unmixed blessing To mention only one consideration the disease caused acute suffering to rabbits, and we could not disregard the humanitarian aspect. Also although the disease appeared to affect only rabbits and to some extent, hares, it was a virus disease and we should surely be unwise to allow a new virus disease to become established in this country without first trying to find out as much as we could about it. The virus affected also of course, tame rabbits. The results of the spread of the disease in Australia and France had, Lord Carrington agreed been spectacular but the final results in either country could not yet be definitely assessed In Australia rabbits were now beginning to appear which were immune to the disease As the rabbit population had been so drastically reduced there would be plenty of food for these immune rabbits to eat. They might well multiply quickly with the result that the Australians would be back where they started with the rabbits and with the disease.

The Minister could see the possible advantage if this disease were to wipe out all the rabbits but he had decided that the problem must be considered carefully and systematically before he could commit himself to a line of action which might have far-reaching consequences He and the Secretary of State for Scotland had therefore set up a committee to consider the problem At the same time the Minister had given instructions that attempts should be made to contain the present outbreaks as far as possible, so as to leave the field clear for the committee to consider the problem objectively It might be that the committee would advise that the disease should be allowed to spread or that it should be introduced deliberately But if this decision were to be taken it would be better that it should be taken deliberately after considering all the evidence rather than be forced on us prematurely by leaving present outbreaks unchecked The committee had endorsed the action taken by the Minister, and the Ministry would be helped in dealing with this problem if farmers and landowners would coöperate by intensifying their efforts to destroy rabbits on their land Myxomatosis even if it spread would give no justification for relaxing our efforts to destroy rabbits by other means. He expected the committee to report before the spring because the disease was likely to spread more in the spring than in the winter when most of the insects were dead or not active.

Shortage of Mental Nurses

In the House of Commons on Nov 12 Mr R. J MELLISH who is a member of the South East Metropolitan Regional Hospital Board called attention to the shortage of nurses in mental hospitals, and especially in mental-deficiency institutions. The problem was of national importance, but its extent, he suggested was typified in his own region where the two mental colonies had 500 empty beds due to lack of staff As a result only low grade defectives, for whom little could be done but who had to have institutional care, could be admitted ; and even for these patients there was a waiting list of 472 urgent cases. By improvisation it had been possible only to admit 158 One regional hospital board had suggested that magistrates should be asked to stop making court orders for admission of these cases to an institution Doctors and nurses were anxious to have a share of the high grade defectives who responded to treatment —and when a hospital was over-weighted with low-grade patients, the nurses became frustrated

As remedies for this situation Mr Mellish urged that the wages and working conditions of mental-deficiency nurses should be improved considerably A national press campaign was needed to attract more people as part time or full time volunteers. There must be no further call up of student male nurses. The Minister must provide special staff accommodation and facilities for recreation particularly in mental colonies in remote areas

Miss PATRICIA HORNSBY-SMITH parliamentary secretary to the Ministry of Health agreed that the gravity of the problem called for national action The number of patients, she continued had risen from 47,010 in 1949 to 53 066 in 1952 At the same time as these patients had been absorbed the waiting lists had risen from 5316 to 0300 In the mental hospitals there were at the moment 137 039 patients resident and overcrowding, she was sorry to say was at the rate of 14 7% In the country as a whole 615 more beds had been opened and the Minister was insisting that the mental health service should have a fair share of the money available to the regional boards

The estimates for 1953–54 included schemes for 1314 new mental-deficiency beds and 007 mental hospital beds. In 1954–55 there would be a special allocation of £1 million the Mental Million which the Minister had insisted must go over the normal allocation of the boards, to the mental side. Through this programme they hoped to provide 1200 mental-deficiency beds and 800 mental hospital beds. In addition to these two programmes three large centrally financed schemes from other funds for mental-deficiency hospitals would provide 800 beds within three years Within the next five years, this plan should provide 3000 mental-deficiency beds and 1500 mental-hospital beds It would, however be some years before all the backlog could be absorbed

But the main problem over and above accommodation, she agreed, was the shortage of nurses Although the number of mental-deficiency nurses had increased from 3812 in 1948 to 7676 in 1952, it was still well below what we needed She would report to the Minister of Labour the suggestion that there should be no more call-up of nurses for National Service The Minister had decided that in the campaign for the recruitment of nurses the bulk of the money should be used essentially for publicity and recruitment for mental nurses In coöperation with the Ministry of Labour and National Service there was to be a programme of local campaigns to encourage people to help their own local colony The proposal of the Standing Mental Health Advisory Committee that nurses on the general register, after a shorter period of training, could be admitted to the mental nursing register, was under discussion with the General Nursing Council Several experimental schemes were under consideration or in operation whereby nurses might qualify for admission to both the mental and general parts of the nursing register in a reduced period They hoped by these means to induce some of the nurses on the general register to enrich their training and enter the mental side The main object was to make the mental-nursing training sufficient for the highest posts in mental nursing At the moment nurses needed the full double qualification before they could become matrons The Minister had appointed for the first time a male and a female mental-nursing officer to the Ministry staff Rates of pay were under consideration by the Nurses' and Midwives' Whitley Council, and it had been urged on them that the rates should be made more attractive But she believed we must also get a new outlook on the part of the public so that parents no longer deterred their children from taking up mental nursing by saying "Nursing, if you must, but general nursing and not mental nursing" People must realise that "there is as great and fine a vocation in nursing those who have sick minds as in nursing those who have sick bodies"

QUESTION TIME

Fog-masks

Replying to a question, Mr **Iain Macleod**, the Minister of Health, said that he was advised that in the present state of knowledge no mask which people could be expected to wear for long periods was likely to give complete protection, but that some types of mask might help those most likely to be affected by smoke polluted fog—namely, people suffering from existing disease of the heart or lungs. He was, therefore, proposing to enable doctors, if they felt it to be desirable, to prescribe under the National Health Service specified types of mask for patients suffering from these conditions who lived or worked in an area where smoke polluted fog was likely to occur The necessary regulation would become effective on Nov 17, and masks should normally be available under the N.H S

Condemned Meat

Mr **Barnett Janner** asked the Minister of Food whether he was aware of the anxiety felt by sanitary inspectors over the auctioning of meat condemned as unfit for human consumption, that such meat might be made available for human consumption in the way of manufactured food products, and whether, in the circumstances, he would re examine the present system relating to such sales —Major **Gwilym Lloyd George** replied I have given careful consideration to the representations which I have received on this matter and have decided to make certain changes in the present arrangements for the sale of condemned meat from Government slaughter houses

I should explain that it would be an offence under the Food and Drugs Act to offer condemned meat for human consumption and that responsibility for the enforcement of this provision rests with the local authorities in carrying out their statutory duties All condemned meat sold by the Ministry is stained green before it leaves the slaughterhouse and local authorities are notified of the names and addresses of the buyers Local authorities are given the right of access to Government slaughterhouses and it is being made clear to them that notwithstanding Crown right their inspectors may take any meat unfit for human consumption and dispose of it as they think fit I am also revising the present conditions of sale of condemned meat from Government slaughterhouses by requiring that before condemned meat is sold retail it should be sterilised

Dr **Barnett Stross** Could the Minister tell us what the process of sterilisation is that is contemplated?—Major **Lloyd George** Boiling for an hour

Myxomatosis

Major W J **Anstruther Gray** asked the Secretary of State for Scotland how far the disease of myxomatosis had been reported among rabbits in Scotland.—Mr **James Stuart** replied I have received no reports of outbreaks of the disease in Scotland, but the North of Scotland College of Agriculture are conducting experiments with the virus on a few small islands

Mr **Somerville Hastings** Is the Minister convinced that this disease can be confined to an island and will not spread to the mainland?—Mr **Stuart** That is the advice which I have received I think that that is the case I hope so

Nerve Gases

Replying to a question, Mr **Duncan Sandys**, the Minister of Supply, said that no complete antidote had yet been discovered to nerve gases A partial antidote had been found, but it was not regarded as wholly satisfactory

Accommodation for Mental Defectives

Replying to a question, Mr **Macleod**, Minister of Health, said that the numbers of mentally defective patients on local health authority waiting lists on Jan. 1 last for England and Wales were 3527 urgent and 5461 non urgent

Territorial Doctors' Car Allowances

Replying to a question, Mr **Antony Head**, Secretary of State for War, said that he had already had evidence that some of the present rates of allowance for use of their own cars on Army business by doctors doing Territorial Army service were causing dissatisfaction, and he was giving consideration to that problem

Caponised Cockerels

Lieut Colonel W H. **Bromley Davenport** asked the Minister of Agriculture what advice he had received from his scientific advisers on present-day methods of caponising cockerels, what severe biological changes resulted in birds so treated, and what steps had been taken to ascertain what were the consequences of the heads, necks, and offal of such birds being consumed in large quantities by pigs—Mr G R H **Nugent** replied The Ministry is advised that the chemical caponisation of cockerels by means of synthetic female sex hormones is a satisfactory method of producing good quality table poultry The effect of the treatment is to arrest the development of the male characteristics of the bird It is recommended that the treatment should be discontinued a fortnight before slaughter, and that waste products and offals of birds that have been subjected to this treatment should not be fed to any class of livestock including pigs. This advice is based on an assessment by our scientific advisers of the results of investigations in the United States. There have been, so far as I know, no such investigations in this country

Lieut Colonel **Bromley Davenport** asked the Minister of Food what evidence his scientific advisers had to show that the consumption of caponised cockerels had an adverse effect on the consumer —Major **Lloyd George** None, Sir

Junior Hospital Medical Staff Appointments

Mr **Roy Mason** asked the Minister of Health what action had already been taken in reply to recommendations made to him by the chairmen of the hospital management committees of the Sheffield Regional Board, what other points were under consideration, and what action was contemplated. —Mr **Macleod** replied Two of the recommendations on junior hospital medical staff came from the chairmen of the board's hospital management committees, one on scales of remuneration and one suggesting the employment of experienced medical officers to supervise work in casualty departments The question of remuneration is before the appropriate Whitley Council as regards the second point, I have indicated to hospital boards that I am prepared to approve the appointment of casualty officers of senior standing in appropriate circumstances I am discussing with the profession other aspects of the shortage of junior hospital medical staff but I am not yet ready to make a statement

Proprietary Medicines

Dr STROSS asked the Minister how many medical preparations listed in the *National Formulary* were dearer than the proprietary brands of the same preparations —Mr MACLEOD replied: Of preparations in common use in general practice the cost to the Health Service of the following 18 is greater than that of their proprietary equivalents 10 others may be dearer according to which of the equivalent products is prescribed or the size of the pack from which it is dispensed

Tab mepyramin. maleat *N F* 100 mg
Tab succinylsulphathiazol. *B.P*
Tab pethidin. hydrochlor *B P* 50 mg
Tab. æthinylœstradiol. *B.P* 0·05 mg.
Tab æthinylœstradiol *B P* 0·1 mg.
Tab. ergotamin. tart. *B P C*
Tab. ferr sulph. co. *B.P C*
Tab œstron. *B.P* 1 mg
Tab æthisteron *B.P* 5 mg
Tab acetarsol *B.P* gr 4
Tab stilbœstr *B.P* 0 5 mg
Tab promethazin. hydrochlor *N F* 10 mg
Tab amidon. hydrochlor *B P C*
Tab butobarbiton *B.P C*
Tab phthalylsulphathiazol. *B P C*
Tab sulphadimidin. *B.P*
Tab hexœstr *B.P* 1 mg
Tab thyroid *B.P* gr ½

Cost of N H.S Prescriptions

In answer to a question Miss PATRICIA HORNSBY-SMITH gave the following figures for the number and cost of prescriptions in the National Health Service in England and Wales for September, 1953

Number (declared by chemists)	16 524 000
Estimated prescriptions per form	1 72
Estimated cost per prescription	47 80*d.*

Charges for Surgical Appliances

Mr GEORGE THOMAS asked the Minister how much he had saved by the imposition of a charge on surgical shoes rupture belts, and elastic stockings. Mr MACLEOD replied I estimate roughly that since the introduction of the charges the annual cost to the hospital service of these articles has been reduced by about £400 000 I am looking into the position of elastic hosiery supplied on the prescription of general practitioners.

Cost of the Social Services

Replying to Dr STROSS Mr J A. BOYD CARPENTER, financial secretary to the Treasury said that the cost of the social services in terms of a percentage of the national income for 1938–39 was 12% and for 1952–53 17%

Prostitution and Male Importuning

Replying to a question, Sir DAVID MAXWELL FYFE said that he had for some time been concerned about the problems of prostitution and of importuning by male persons in London, though he thought it important to view this matter in a proper perspective and not to draw exaggerated pictures of the extent of the evil to be found in the streets He had, therefore been anxious to obtain advice and information from various quarters, including information about the law and practice in other countries, which might help in considering whether any amendment of the law, or any changes in the present methods of enforcing the law would be likely to help in dealing with the problem, As part of these inquiries, he had arranged for an assistant under secretary of State in the Home Office and a commander of the Metropolitan Police to visit the United States He had recently had a discussion with some of the Metropolitan magistrates who dealt with cases of this kind arising in the West End with a view to getting first hand knowledge of their impressions and experience He did not of course seek to advise the magistrates how they should deal with particular cases coming before them He was studying various aspects of these problems but he had no further statement to make at present

Fees for Cremation Certificates

Replying to a question Sir DAVID MAXWELL FYFE said that the British Medical Association had advised doctors that a suitable fee for the completion of either certificate B or certificate C for cremation was two guineas plus a mileage allowance where applicable at the rate of 1*s* per mile, or part of a mile, each way outside a radius of two miles. In view of this action he did *not propose* at present to make use of the power contained in the Cremation Act 1952 to prescribe maximum fees.

In England Now

A Running Commentary by Peripatetic Correspondents

'WHY must your weekly medical journals be so dull ? '

I looked up from my scrutiny of one of the journals to see my wife idly turning over the pages of the other one

I don t think they are so dull, dear

Well I suppose that it s all right for you But considering that every medical household in the country probably takes at least one of them if not both I think they might cater for the family a little more

But they are not really supposed to be for the family

Well, they should be.'

After that piece of unassailable feminine logic the discussion could proceed no further but I began to wonder if there wasn't something in what she said There is the *Family Doctor* of course, but that is hardly the same thing Something more like the *Doctor's Family* would be needed

There would have to be a Woman Doctor s Page with fashion notes on natty two piece dark blue suits, hints on how to get help when the car breaks down, and easy recipes 'for your husband to make " The school-children could have their growing minds trained along the right lines by a comic strip: *The Adventures of Lionel Scalpel—Medical Student* sounds exciting Lionel would get himself involved in all sorts of thrilling incidents—trapping the porter who is stealing the precious supplies of cortisone discovering that the mysterious patient in Surgical 2 is a Russian spy who is after the Senior Surgeon a prominent Territorial officer and so on

An advice column, run by an understanding sympathetic, but sensible Auntie would have plenty of material A young house-surgeon is in love with the new theatre sister and is jealous of the surgical registrar who seems to be paying her a lot of attention; what should he do ?

Even the Original Articles could be brightened The longer ones could be serialised, breaking off each week at the beginning of an exciting development, with a little note in the approved manner at the end of each part—'Will methylphenylpolysyllabalate reduce the blood pressure ? Is it toxic ? How many patients were treated ? Don't miss next week s thrilling instalment !

* * *

A harassed steward last week notified our pathological department that the dietitian had received an order for 8 fertile eggs a day for a patient. If eggs were sent from the kitchen, could the pathological department please fertilise them ? At the time the pathologist was reading an article by Dame Harriette Chick, but felt that not even this eminent authority on nutrition would be able to help A colleague suggested that Sir John Cockcroft might be approached We wonder why the request came to us: of course we have a Henman on the staff

* * *

A consultation in Bermuda is something to dream about. It is also one of the few experiences that make an exception to that great law to travel hopefully is better than to arrive ' Arrival at 3 A.M. in a tropical night meant being greeted by a continuous chorus of singing (sic) tree frogs and a pleasant journey across the island in a 10 H P car (the largest allowed) at a speed which kept strictly to the universal limit of 20 M P H Speed traps are plentiful and radar-controlled and there is no argument.

A swim in the sea at 70 F was followed by a sleep—and then an awakening to a vision of deep blue sea and sky scarlet and green trees, pink beaches, and honey coloured rocks That day I met my American colleague. Well now my name s Bill we've got a little party this evening for you so s you can get the atmosphere before talking shop

At the consultation I was for once at a much needed advantage Complicated laboratory tests or unusual investigations were impossible, and my American friend felt that a complete diagnosis that had not gone fully into all possibilities was uncertain; for he tended to trust investigation more than experience Similarly he considered management almost impossible on general principles of medicine alone, without "getting under your patient's hide" by living with him for at least 48 hours *Just as certain English humour is difficult for Americans by reason of its understatement, its mental short-cuts, and its reliance on implication, so it seems difficult for them to understand how, for example, a firm diagnosis of disseminated sclerosis can be reached without even a lumbar puncture* But our discussions taught me that this type of American medicine is painstaking, thorough, and comprehensive, and that a strong thread of common sense runs through it

I left this beautiful island with regret, and I wish I had seen it before cars were allowed there and before those beautiful red cedars were destroyed by a scab imported on a rare plant brought in by an American millionaire Re-afforestation, I was told, will take ten to twenty years As the plane circled the island I thought of the haunting calypso rhythms, the brightly coloured trees, the taxi-driver who stopped just to pick me a night-blooming cereus flower, the solemn-faced, clean, gaily dressed coloured children with their English accents and their passion for cricket, and above all the lovely warm bathes in the early morning

Ah, well, it all seems like a dream I must go and do a domiciliary

* * *

The other day a young woman of our acquaintance saw her five-year-old son off to school for the first time This is a time fraught with emotion for any mother, and she felt as sad as most as she returned indoors to wait for midday and his safe return Would they be kind to him? Would he be good? Would he be miserable? At noon home he came, hair smooth, knees ungrubbied, and to all outward appearances unchanged Our friend heaved a sigh of relief and was about to get on with the lunch, when a hand caught her skirt and a small trusting voice demanded, "Mummy, where did I come from?" Changes with a vengeance! However, she is a sensible girl, so she sat down and explained the facts of life with simplicity, ease, and a commendable lack of self-consciousness Towards the end of her story she noticed a slight wriggling and slackening attention, so she stopped to ask what had prompted the question "Well, I just wondered as we hadn't been here always and the boy who sat next to me came from Guildford"

* * *

The obstetricians are understandable with their D.M.P., E.U.A., Z.A., D.E.D., and B.B.A.'s The X-ray man's N.B.I. makes sense too, but B.A.P.W.O. & P.P.D. which is the E.N.T. H.S.'s only report on *my Jimmy Jones is* N.B.G. to the poor G.P. and G.O.K. what it all means

* * *

MILLI EQUIVALENTS

Thoughts on reading recent correspondence in THE LANCET

The electrolyte shines fiercely bright
  in every tissue cell
The white haired sage turns the textbook page
  but it doesn't ring a bell

His youth was spent among grammes per cent
  he knows nought of equivalents milli
' I must be up to date, but I can't equate,
  these radicals drive me silly "

I've lost my way with Na and K"
The tears roll down his cheek
More sodium loss, I don't care a toss
The future is so bleak"

The cations call from the boundary wall
  at an anion stuttering by
The acids race to reach their base
  while the fluid's flying high

The Clinician groans at the Lab Man's tones,
  he gives a despairing yell
The electrolyte shines extremely bright
  but it's now a padded cell

Letters to the Editor

THE INSULIN MYTH

SIR,—Dr Bourne (Nov 7) has done well in destroyi the myth of the cure of schizophrenia by insulin Havi treated schizophrenics for many years by various method I have now no doubt that those who recovered aft being treated by insulin recovered in spite of the trea ment and not because of it, and I am relieved th I no longer submit my patients to a treatment so unplea ant, dangerous, and useless Diagnostic and prognost problems so perplex those who deal with this disea that figures of recovery rates are apt to become expre sions of personal bias, and, for my part, I am convinc that most acute young schizophrenics recover natural from their first attack and many from a second, recover which usually occurs within a few months, may ta place after times varying from a few days to seve years Any treatment given to these patients is like to be hailed as specific by the over enthusiastic. As t treatment of schizophrenia by insulin does not increa the rate of recovery, shorten the duration, or preve recurrences the method should now be consigned to t dustbin of therapeutic failures The patients will th have less unpleasant memories of their time in hospital.

For chronic schizophrenics electroconvulsion thera may assist in relieving them of some of their sympto and in making their lives less turbulent, but bett results can be got where patients are well nursed b an adequate staff under pleasant conditions, and whe this is done E.C.T. is unnecessary

J GIBSON

Gloucester

SIR,—May I join issue with Dr Bourne in defence a treatment whose relegation to the realms of psychiatr mythology is surely premature?

I think it is unfair to judge the value of any treatme applied to chronic cases, so I would disagree that t effects of insulin in chronic schizophrenics could ever b used as a basis for estimating its efficacy Analogousl one would hesitate to assess penicillin by its effect chronic infections in which tissue changes had alread occurred In chronic schizophrenia, morbid reactio patterns are already established and are notoriousl difficult to influence in a lasting way by any treatment.

Turning to early cases, Dr Bourne has rightly empha sised the peculiar difficulties of assessing the results any treatment in a condition like schizophrenia. Th virtual impossibility of obtaining adequately matche control groups is not surprising in a syndrome (on hesitates to say disease) so protean in its manifestatio Within these limitations, however, numerous invest gators have reported better results with insulin than wi routine hospital care or E.C.T. in large groups of subjec Because of the lack at present of objective diagno criteria, their results are always open to arguments suc as Dr Bourne has advanced

One might, I think, compare the present state treatment in psychiatry with that in medicine a centur ago Our relative ignorance of ætiological factors or th natural history of the disease in many cases of schiz phrenia forces us into an attitude of empiricism Insuli treatment is one of the most powerful methods at ou disposal for altering both the internal environment an the relationship between the patient and his helpers. I we cannot be quite certain that insulin does not preve patients from subsiding into "this most stagnant conditions," we should give the patients the benefit the doubt

Cane Hill Hospital,
Coulsdon Surrey

F B. CHARATAN

SIR,—The paper by Dr Bourne indicates that co troversy still persists, twenty years after Sakel's origina discovery, over the value of the deep insulin treatment schizophrenia Dr Bourne appears to me to base his arguments against the efficacy of insulin on three points first, that there is no proof that a similar number of untreated cases would not get well spontaneously second, that E C T is as good or better than insulin and third, that the character of mental disorder may be changing in favour of a more benign type of schizophrenia

Commenting on these points in their reverse order there is as far as I know no statistical evidence that the severe forms of schizophrenia are diminishing in numbers What we may be seeing is a larger number of schizophrenic breakdowns in which environmental causes and emotional stress play a larger part than hitherto With regard to the second point, one would have thought that there is by now adequate evidence that the results of insulin are better than those of E.C T in schizophrenia the work of Linford Rees may be selected as an illustration. Furthermore one believes that at most hospitals E C T is given before insulin in the treatment of schizophrenia, the reasons for this being that insulin treatment is more prolonged and also more dangerous

Dr Bourne s first point is the one on which any attempt to evaluate insulin treatment must turn He points out that there are indeed many variable and unknown factors in assessing the results of any treatment and until there is conclusive proof that the chronic schizophrenic population of mental hospitals is diminishing in relation to the total population of the country we cannot be certain that the physical treatments are really effective in the long term management of the psychoses Although I have no figures to hand I am certain that insulin not only shortens the average period of stay in hospital but that it also prevents relapse and lowers the readmission rate. The following summary of the figures at this hospital since an insulin unit was opened for the first time early in 1952 may be of interest

Fifty-six patients have so far been treated All were suffering from schizophrenia Two patients did not complete the course and one died. The remaining fifty three all had at least 40 comas, except for one patient who recovered and has kept well after 20 comas. Forty three of these patients are out of hospital and are known to be holding their own although in nine cases the ultimate outcome is thought to be doubtful and some of these are not working

Of the ten failures, two have subsequently been readmitted to other hospitals, two have recently been readmitted here and the remaining six have stayed in the hospital since treatment was completed Of the forty three patients discharged, one had a leucotomy after insulin had failed and her recovery may be attributed more to this than to the insulin Therefore, out of fifty three patients, thirty three or about [illegible]% may be said to have recovered after a course of insulin treatment. In eighteen of these cases insulin was successfully given after a course or courses of E C T had failed. We thought that about twenty-seven of the patients were suffering from dementia præcox and would not have recovered without treatment, while in a further eight cases recovery was regarded as doubtful unless insulin had been given. Thus a so-called spontaneous-recovery rate of between 35% and 50% only could have been expected from this group and then the period of stay in hospital would undoubtedly have been much longer Those who congratulate themselves on the fact that the schizophrenic patient has recovered spontaneously probably do not consider the extent to which schizophrenic morbidity exists These patients, although at home and working lead restricted, poorly adapted lives, often continuing to indulge in psychotic fantasies.

Most of us who are experienced in insulin treatment would agree that the quality of the insulin remissions is much better In 1947 I reported[1] on 303 schizophrenic patients treated with insulin. 60% of the 61 patients that had been followed up for more than five years were still out of hospital—a figure which compares favourably with the present recent series.

We must further ask ourselves whether about 40% of schizophrenics would remit spontaneously if kept at home, supposing this were possible on social grounds. Is it indeed true that ‘ few mental hospitals, even today are able to offer recently admitted patients much more than custodianship rug making the cinema, and a chat every week or two with the doctor ’ as Dr Bourne asserts? The serious shortage of medical staff in most mental hospitals may limit psychotherapy but a grave injustice is surely done to the part which the nursing staff and the general discipline and atmosphere of the hospital can play in helping the patient particularly where the patients in the hospital are organised on a group basis. Furthermore most progressive mental hospitals can now offer a range of treatments which is impressive compared with even twenty years ago

There is great need for some criteria concerning the depth and duration of coma in insulin treatment. Psychological studies show that nearness to death is an important factor in recovery from schizophrenia. It is of the greatest importance that insulin treatment should be adequately carried out, with each coma carefully supervised to allow the patient to become as deep as possible without serious danger to life We might also do well to avoid thinking in terms of ‘ physical as opposed to psychotherapeutic, treatments If psychotherapy assists in the recovery of our insulin patients let us use it even if it upsets the figures of the statisticians

Dr Bourne rightly asserts that the recovery rate in early schizophrenia is higher than after the disease has become established. It seems to me that the only way we shall persuade early schizophrenics and their relatives that hospital treatment is necessary is by offering them some definite form of treatment. One would welcome any new approach either on an outpatient or inpatient basis, which would help to deal with this grave problem To attempt to dissolve a treatment which is widely accepted as the best weapon we have into a myth appears to me a retrograde step

In view of the confusion which still exists regarding insulin treatment, I would like to suggest the formation of a small professional committee possibly under the ægis of the Royal Medico Psychological Association, to inquire into the present state of insulin treatment in mental hospitals and the results that are being obtained

Powick Mental Hospital
near Worcester　　R A SANDISON

THE LETHAL AEROSOL

SIR —Your articles on fog have been most instructive and if taken in conjunction with the demands of the Local Medical Committee for the County of London should lead to decisive action

There seems little doubt, as you suggest that the sulphur laden aerosol in cold weather is responsible for much respiratory damage. I would like to describe what I think is a perfect mechanism for making such an aerosol I live 300 yards upwind from a large power station As dawn breaks one can watch a billowing cloud of cooling steam float from the cooling towers This often extends across the sky for two or three miles into it the power station chimney belches huge quantities of unwashed smoke and grit. Under favourable weather conditions this goes on for hours the sun is blotted out and a drab half light replaces its rays On other days we are not so fortunate for the water vapour descends on the main road and brings traffic almost to a standstill

There is an increasing number of power stations in Greater London. Within a radius of one mile, Fulham, Lotts Road and Battersea consume 2 000 000 tons of coal a year Can we wonder that Westminster and County Hall were the centre of last year s lethal smog? Can Westminster Abbey be saved while being subjected to such continuing sulphur baths?

The remedies, Sir seem fairly simple. May we hope that too many committees do not obscure the issue and delay action

London, N W 10　　HORACE JOULES

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[1] Sandison R A *J ment Sci* 1947 93 29

VAGARIES OF INTELLIGENCE

SIR,—We note that Sir Cyril Burt, in his letter of Nov 7, does not disagree with the main general conclusion of our article He confines himself to removing "one or two *misconceptions,*" some of which seem (if we may say so) to be of his own creation

He states that the criticisms we made of the I Q are by no means new, and asks who has ever disputed I Q variability Surely he must be aware that there is a widespread belief, both in uninformed and informed circles, that the I Q, as currently used, is virtually constant, and this belief is supported by many reputable textbooks

He makes the important statement that the formula for calculating the I Q, suggested by himself and others, is based on a fallacy—i e, that the changes in mean mental age and in the standard deviation are rectilinear, whereas in fact they are curvilinear He then goes on to say that this formula is the main cause of I Q inconstancy, but that it can largely be corrected by "adopting a more complex formula" He does not mention such findings as those of the Harvard Growth Study, the results of which are not expressed in terms of the usual I Q formula, but as observed means and observed distributions Does he seriously suggest that the changes in intellectual status demonstrated by Dearborn and Rothney, or even in our own small experiment, are mainly statistical artefacts ? In the latter study it was quite clear that those who had made the larger I Q increments could deal more effectively with reality, as sampled by their greater success in solving objective and standardised test problems In addition, of course, the Wechsler test overcomes the difficulties implicit in the use of the conventional I Q formula, as is indicated in Dr Wechsler's book on the subject

Sir Cyril says that we criticise previous views, including his own, and he quotes us as saying "These investigators . . . rarely, if ever, submit their hypotheses to experimental proof" He has omitted the key phrase of the sentence, which reads "These investigators, *however, while offering hypothetical explanations for the changes in intellectual level which they demonstrate,* rarely, if ever, submit their hypotheses to experimental proof" He thus implies that we criticised himself and others for not proving I Q inconstancy, on the contrary, we quoted his experiment as supporting our thesis Our only criticism, as the full quotation clearly indicates, is that the investigators, having demonstrated the fact of I Q variability, failed to take their work a stage further by verifying the often important hypotheses which they advanced to explain it (For example, "some happy change in home conditions seemed responsible" for some I Q increments, was one of Sir Cyril's own hypotheses)

Sir Cyril observes that one reason for I Q inconstancy is that so many who employ intelligence tests "have never been trained in their administration and interpretation" This is undoubtedly (and very unfortunately) a feature of some administrative and clinical practice, our article, however, confined discussion to researches carried out by well-established psychologists He also points out that no trained psychologist "relies on tests alone—much less on a single test—in any doubtful case" Unfortunately, however, decisions about an individual's future are sometimes made (whether the psychologist likes it or not) by the authorities concerned, on the basis of a single test score, which may have been assessed by someone with the lack of training which Sir Cyril properly deplores, and under conditions which may be by no means ideal

In brief, it is not infrequently observed that bright children may in time show less promise than had been hoped, or that dull children may sometimes blossom to a level which surprises those who knew them Individuals are not static, but capable of change, within limits which are as yet imperfectly understood. We are sure that Sir Cyril will agree that we need to identify the factors which influence such changes, in order t play a more positive rôle than that of passive spectators who merely record them as and when they occur

Manor Hospital
Epsom Surrey

A D B CLARKE
A. M CLARKE.

MOLLUSCUM PSEUDOCARCINOMATOSUM

SIR,—In your leading article of Oct 17, you state tha confirmation of the occurrence of this condition in othe countries would be welcome

I am indebted to a dermatological colleague, Dr A D Muir, for calling my attention to the condition abou two years ago, and I was able to show 5 examples at th meeting, in May, 1952, of the Pathological Society New Zealand During the past fourteen months I hav made 27 such diagnoses, and I have raised the possibilit a further 17 times (The histological differentiation fro squamous cell carcinoma of the lowest grade of malignancy or from some hyperkeratoses is not always possib on tiny biopsy fragments) Without knowledge of th condition I would have (and in the past had, in fact diagnosed many of these as squamous cell carcinomata about a 100 examples of which were seen in these fourtee months The follow-up records of the local cancer clini confirm a number of such misdiagnoses

These rough figures support both the quoted frequenc of the condition and your concluding remark tha "statistics of incidence and prognosis of skin cancer wi need to be drastically revised"

Public Hospital,
Christchurch, New Zealand

D T STEWART
Director of patholog

TEETHING

SIR,—I read with interest the remarks of one of you peripatetic correspondents (Nov 7) on the placeb I could quote one or two cases from experience tha would require him to deal with "teething" under th heading of the placebo in its ecclesiastical and not m medical sense

Quite a lot has been known for some time about th histological, anatomical, and morphological details o normal eruption of teeth In the natural history o eruption,[1] there is one point at which trouble may an often does arise, and it is easy to understand why A the tooth approaches the surface in the mouth the cr epithelium fuses with the enamel epithelium of th tooth, immediately before the crown of the tooth emerges, this combined epithelium breaks down in th centre and is absorbed—and thus the tooth is exposed For some time before actual eruption there is therefore a thin layer of soft tissue between the crown of a har tooth and any hard object the child may bite upon

In the case of the first and second deciduous molars which are square and flattish teeth and which normally erupt at about one and two years respectively—when th child should be biting hard objects and trying out i dental apparatus—there is usually irritation of th overlying epithelium and sometimes they actually mast cate this piece of themselves Local inflammation i common and a vicious circle may arise

Instinctively the child seems to bite upon the irritation t relieve it, with anything it can lay its hands on or get i jaws near While actually applied, pressure does seem t give relief But it also increases the inflammation and wh was bad becomes worse The crying increases and the bab gets tired—and tired, cries the more Soon it becom exhausted and another vicious circle begins It is not th local condition that is usually serious (though it can be) b the fatigue that this trivial matter causes—and worse, th bad habits that may have their origin in the fuss that acco panies the bad tempers of a tired and crying baby and tired and anxious brace of parents, especially if it is the

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1 Toller, J R *Brit dent J* 1948 84, 255 *Ibid,* 1948 85, 1

first baby. Unfortunately the doctor can rarely be sure that the trouble is only a tooth coming through and his uncertainty is communicated to the parents, who are anxiously appraising every sniff the child makes. The parents expect their doctor to be omniscient and cannot appreciate (anyway on these occasions) that clinical pædiatrics and veterinary science have much common ground. The sedatives that the wise physician orders for all concerned—baby, parents, and himself—if he has been called out in the early hours, are the best and only possible treatment.

Your correspondent, I feel, may go on using 'teething' as a diagnosis. Very often it will be the right one. Until I had babies of my own I dismissed 'teething' as an old wives' tale.

And one must always bear in mind accidents of eruption. A cyst of eruption may break down and become infected. These cysts are more frequent than is commonly realised. I have seen severe cases of Vincent's angina focused around an erupting first permanent molar in the mandible. The troubles of erupting third molars—or of third molars that cannot erupt—are well known.

Cambridge. J. R. TOLLER.

RECURRENT PAROTITIS

SIR,—It is highly probable that, contrary to the impression given in your annotation of Sept. 26, only a few cases of recurrent parotitis of childhood are caused primarily by bacterial infection. Mention should be made of another condition called periodic sialorrhœa. This is a curious disorder of unknown origin in which the salivary glands swell at regular or irregular short intervals over many years. The swelling is accompanied either by xerostomia or sialorrhœa. We have described[1] a case and referred to others that have been reported.

While it is possible that secondary infection with pneumococci or staphylococci may occur in such cases and require treatment, much unnecessary surgical treatment for the removal of supposed foci of infection and unnecessary and possibly harmful massage and antibiotic therapy could be avoided if correct diagnosis were made.

American University of Beirut,
Lebanon.

HOBART A. REIMANN
Professor of Medicine.

ALL IN THE DAY'S WORK

SIR,—It seems, from his Widdicombe letter last week, that Dr "Bill Brewer" is going to do side-room tests not only for his own patients but for those of his partners. Will he not get bored with this? Most practitioners find a certain satisfaction in themselves completing the examination of their patients, including these simple tests; and thereby they get a better grip of the case. Where the responsibility is divided the partners will have to exchange written notes requesting and reporting on a test; which wastes time. The patient's time may also be wasted: supposing that the hæmoglobin is to be estimated with the M.R.C. grey wedge hæmoglobinometer, the patient will attend one doctor, be referred to Dr Brewer for the test, and then have to come back the next day for the result. Why not use a Sahli hæmoglobinometer? Then the test can be completed by the patient's own doctor in a few minutes. This method is quite accurate enough.

Is not Dr Brewer a little audacious in proposing to diagnose pernicious anæmia from the appearances of a film alone? After all, on his findings may depend whether the patient attends for injections monthly over the next twenty years. It seems a pity, too, that he is not going to do white-cell counts. These help greatly before starting to treat pneumonia or pleurisy, and also sometimes in acute abdominal disorders; and occasionally they bring to light a case of acute leukæmia.

G.P.

THE R.M.B.F.

SIR,—I venture to remind your readers of Lord Webb-Johnson's Christmas gifts appeal published in your issue of Oct. 3.

The distribution of gifts is made well in advance of Christmas Day and I earnestly hope that those who have not yet responded to the appeal will send their contributions as soon as possible to the Secretary of the Royal Medical Benevolent Fund, 1, Balliol House, Manor Fields, Putney, London, S.W.15, marked "Christmas Gifts."

FRANK JULER
Honorary Treasurer.

DIARRHŒA AFTER GASTRECTOMY

SIR,—Mr Williams and Mr Pullan (Nov. 14) sometimes found it necessary to give their patients suffering from necrotising enteritis 9 g. of sodium chloride and 3 litres of water in an hour. To do this, they infused 1 litre of physiological saline solution and 2 litres of 5% dextrose solution. In your leading article on the subject you state that treatment consists in "the infusion of glucose-saline solution in large quantities—sometimes as much as three litres an hour." This is three times as much sodium chloride as Williams and Pullan were using, whether it be measured in grammes or in milli-equivalents.

A dehydrated patient requires either water or salt and water, and 5% dextrose solution and/or physiological saline are used to make good the deficiency. The amount to be given and the solution to be used depend on the needs of the individual patient. If these are in doubt, the writings of Marriott should be consulted. Dextrose-saline is not a compromise: it is a hypertonic solution containing 0·9 g. of sodium chloride and 5 g. of dextrose in each 100 ml. and it will quite soon produce thrombosis of the vein, and œdema in a patient who is not deficient of salt.

Mr Richardson, Dr Billinghurst, and Dr Vere (Sept. 19) treated a patient who had an adynamic ileus. After five days, during which time the patient "received water only by mouth and 5% dextrose intravenously," there was sacral œdema and the serum-sodium level was 148 m.eq. per litre. 3897 ml. of fluid was aspirated from the stomach and 8790 ml. of urine was passed. The ileus was still present on the fifth day; there would, therefore, be a considerable amount of fluid containing sodium in the small intestine. Some salt, also, must have been lost in the sweat during those five days. Yet on the fifth day this patient had too much sodium. I feel sure that the patient during those five days was being given either saline or dextrose-saline.

May I suggest that dextrose-saline solutions should be discarded—except for a few bottles which might be kept for diabetic patients. I have mentioned the effect of this solution on the veins. It also causes inaccuracies in the literature, and confusion among the medical and nursing staff who do not always appreciate the difference between dextrose-saline and dextrose solutions.

Victoria Infirmary,
Glasgow.

JOHN C. GRANT.

ISCHÆMIC NECROSIS OF THE STOMACH

SIR,—I was interested in reading the paper by Mr Rutter last week to note that he could find no published record of this complication during the past twenty years.

About two years ago I performed a post-mortem examination on a patient who died after a subtotal gastrectomy for gastric ulcer. His condition before death suggested strongly that a suture line had parted, but death was in fact due to the condition Mr Rutter describes. The suture lines were intact but the stomach remnant, which was almost entirely necrotic, had a large rent, and tore further on the most gentle handling Neither the surgeon, who was present, nor myself had any doubt but that an excessive number of vessels had been ligated in mobilising the stomach in the course of a difficult operation for a high lesser curve ulcer, and that this had precipitated the condition

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[1] Reimann, H. A., Lindquist, J. N. *J. Amer. med. Ass.* 1952, 149, 1465.

At the time I assumed, wrongly it would seem, that this must be a well-recognised complication, and thought no more about it until I read Mr Rutter's paper In view of his remarks, I feel that you might be interested in hearing of a similar case

United Liverpool Hospitals ROBERT P TOWERS

TUBERCULOSIS

SIR,—In your issue of Nov 7 Professor Francis says that I have tried to show "that as one eradicates tuberculosis from cattle the death-rate from pulmonary tuberculosis increases" This is only partly true my whole theme about the inverse relationship between human and bovine tuberculosis is based on the increase in the *incidence* of the disease in countries and counties with a high proportion of tuberculosis-free cattle I have published [1] figures in your columns which support this view These figures showed a very much greater reduction in human notifications in those Scottish counties with few tuberculin-tested cattle, and this applied to both pulmonary and non-pulmonary disease I have also collected figures from the English counties, and these suggest a similar connection

In my opinion, the recent small increase in notifications of human tuberculosis in England is entirely due to the attested cattle scheme My conclusion is that the consumption of milk designated "Tuberculin-Tested" is not only failing to prevent human tuberculosis in England but is very substantially increasing it

High Wycombe, Bucks L PITCHER

HYALINE MEMBRANE IN THE NEONATAL LUNG

SIR,—From observations made on the microscopical appearances of the lungs in some 600 necropsies on stillbirths and neonatal deaths, I would agree with Dr Claireaux's conclusion, in his interesting paper of Oct 10, that the primary factor in the production of this lesion is aspiration of liquor amnii, and not, as suggested by Dr Emery (Oct 24), a local vascular change in the intrapulmonary circulation But, if hyalinisation of the inhaled squamous cells is a preliminary stage in the formation of the acidophil membrane in the infant's air passages, and if such hyalinisation can be produced experimentally, merely by incubation in normal saline at 37°C, it is difficult to understand why Dr Claireaux states that "*after aspiration*, the squames deposited in the lung undergo progressive hyalinisation" (my italics), for it seems that hyalinisation could occur equally well while these cells were floating in the liquor amnii, also at 37°C, before this is aspirated, unless some other factor promoting hyalinisation is postulated—a factor that operated only after the cells had found their way into the fœtal lung

If, indeed, hyalinisation can occur before the squames are aspirated, it is hard to understand why Dr Claireaux's rat no 7, which received an intratracheal injection of centrifuged deposit from liquor amnii which had not been incubated after collection, failed to show the formation of a true hyaline membrane On the other hand, if Dr Claireaux is right in saying that hyalinisation of squames occurs only after aspiration of the liquor amnii by the fœtus, it is surprising that a widespread, homogeneous membrane can be found in infants dying within only 24 hours of delivery, even though, as Dr Claireaux states, it is likely that many of these exhibit intra-uterine respiration only just before delivery—as in those infants that take a gulp of liquor amnii at delivery by cæsarean section In view of this it would be interesting to know why Dr Claireaux found it necessary to incubate the specimens of centrifuged liquor amnii for as long as 8 days before injection, and whether a true hyaline membrane, as in rats nos. 1, 2, 3, 5, and 6, could be produced experimentally after a much shorter period of incubation

With regard to the staining properties of the membrane, I agree with Dr Claireaux that "often, but not always, neutral fat can be detected" But I have found that sometimes very prolonged staining, often overnight, will reveal a sudanophilic reaction in hyaline membranes which would not appear with normal methods of staining. It is possible, therefore, that vernix is a more frequent, and perhaps more important, component of hyaline membrane than is suggested by Dr Claireaux.

Department of Pathology,
St. Mary's Hospital,
London W 2

W E HUNT

GASTRIC RESECTION

SIR,—Mr Shepherd (Oct 24), in commenting on my article (Oct 10), emphasises the necessity for examination, while the operation is in progress, of the portion of stomach removed and if necessary of the remaining gastric segment Since my article was accepted for publication I have had a case which forcibly, and fatally emphasised this point

A man, aged 53, who was bleeding furiously and was in very poor condition, was subjected to laparotomy No lesion was detected and partial gastrectomy was done There was no ulcer to be seen when the specimen was examined. Bleeding recurred on the following day, and despite further transfusion the patient died some forty eight hours later The pathologist reported finding, post mortem, an acute ulcer less than five millimeters across and situated one inch below the œsophago-gastric junction, the open mouth of a vessel projected from this ulcer

As no fresh blood welled forth during the fashioning of the anastomosis, and none was aspirated from the intragastric tube, it can be assumed that, at the time of operation, the bleeding had temporarily ceased. Despite this it is possible that the lesion might have been detected had the gastric remnant been scrutinised, though I remain unconvinced that so small an ulcer, not actively bleeding, would have been found on gastrotomy, having regard to the much greater area to be examined.

Partial gastrectomy is advised by Mr Shepherd in all cases for which laparotomy has been considered necessary. I think that there are rare exceptions, such as case I in my article, it is in such cases that I regard gastrotomy as of potential value in that disclosure of the lesion as an acute ulcer or an acute erosive gastritis should influence one to spare the stomach Gastroscopy, excluded from the scope of my article, may be of help in these cases, since a finding, as above, would, in my opinion, exclude operation Dr Avery Jones's findings (Nov 7) support this view

Mr Moloney (Oct 24) takes me to task for a "burst of activity" in that I advocate gastric resection rather than gastrotomy when no obvious ulcer is found He goes on to describe his own technique, which involves an incision four to six inches long in the stomach wall, followed by division of the pylorus and opening of the first part of the duodenum, if his investigations are still negative a sigmoidoscope is introduced into the duodenum and sometimes even into the jejunum via a jejunotomy Following this "burst of activity," if Mr Moloney will allow me to borrow his phrase, he concludes that "if no ulcer is found after such methods, and an œsophageal source of bleeding has been excluded, it is fair to do a partial gastrectomy on an empirical basis" This appears to get us back where we started—though considerably later—and it seems to me that had Mr Moloney real faith in his method he would, when it yielded negative results, confidently close the abdomen leaving the exonerated stomach and duodenum to rest in peace.

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[1] Pitcher L *Lancet* 1952, ii 1132

Surgery has an important part to play in the management of hæmatemesis, and in the difficult circumstances of the negative exploration one cannot afford to neglect any suggestion which may be of value to the patient I would be interested to learn more of Mr Lundsgaard Hansen's experience (Nov 7) with Rovsing s manœuvre One must not lose sight of the fact that the operation is done as an emergency measure to control bleeding and I believe that, with careful selection of cases when no obvious lesion is found gastric resection offers the patient a better chance of recovery if performed before rather than after, a series of gastrotomies, duodenotomies, and jejunotomies; consequently I think that when next I operate for hæmatemesis I will, on the whole leave the sigmoidoscope in the cupboard

Hastings.　GORDON FERGUSON

HYPOTHERMIA

SIR,—Your leading article last week suggests that surface cooling, while suitable for children, may not be the method of choice for adults

After watching surgical colleagues using surface cooling in their animal work, I have cooled two well-covered adult females for surgery of the aorta using simply ice-cold wet towels and two electric fans In the second case cooling to just below 30°C took less than $1^1/_2$ hours The simple cooling box ' under which blue children lie during surgery is used, and the method seems both simple and relatively quick when applied to adults

Postgraduate Medical School
of London, W 12.　JOHN BEARD

PREVENTION OF POLIOMYELITIS

SIR,—To return to the mysterious incidence of poliomyelitis and the suspicion that herpes virus may ward it off by having got there first I referred in my letter of Oct. 10 to Burnet s article [1] in which he showed that in Melbourne there was a normal incidence of herpetic infection among poliomyelitis patients and to Weyer s paper [2] which tells a very different story The most relevant passage of Weyer's is

> Of the sera available for examination from the standpoint of herpes antibody as reported above 27 were specimens drawn from children who proved to have been susceptible to poliomyelitis, all of them victims of the 1931 epidemic The bleedings were in most cases initial ones—i.e they were made upon diagnosis of poliomyelitis for the purpose of neutralisation tests with the virus of poliomyelitis. The results of the tests with herpes virus showed them to be individually and collectively devoid of any neutralising effect A comparison of the results with the incidence for herpes virus neutralisation in the same normal age groups gives:

Age group	*No of sera of non-polio patients*	*% neutralising herpes virus*	*No of sera of polio. patients*	*% neutralising herpes virus*
0–5	16	17	12	0
5–10	18	50	8	0
10–15	9	55	2	0
Age ?			5	0

As far as a mere G P can see, the great difference between Burnet's and Weyer's material was that Weyer got his much earlier in the poliomyelitis disease The whole subject could be of such vast importance that it simply weeps for investigation.

Only yesterday I came across a suggestive case history: a man of 21 contracted poliomyelitis, his elder brother had had it at the age of 14 the odds against this happening must be long but if some early influence common to both like the contracting or not contracting of herpes were a necessary factor for getting poliomyelitis the odds are much shorter

Beckley Rye Sussex.　C G LEAROYD

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1. Burnet, F M., Lush D *Lancet*, 1939, i 629
2. Weyer E. R. *Proc Soc. exp. Biol. N.Y* 1932 30 309

LACTIC ACID IN THE TREATMENT OF OSTEO ARTHRITIS

SIR,—The paper by Dr Lawrence (Oct 31) purports to be an objective analysis of 100 cases of osteo-arthritis of various joints; all the patients had physiotherapy and half of them were in addition, given injections of lactic acid. On the surface, the argument appears impressive but on closer examination it can be seen to contain a number of faulty assumptions sufficient to vitiate its conclusions

Dr Lawrence criticises the reports of treatment by myself and others mainly because there was "no comparison with other methods of treatment or with untreated cases ' At the risk of implying a ' tu quoque ' I must confess that for many years I have sought without success for a statistical account of the relative values of the different forms of physiotherapy in treatment and return to work—the only really valuable criterion—although many hundreds of thousands of patients must have been so treated: so the charge rebounds

There is a lack of precision in some parts of Dr Lawrence s article He says that ' standard methods of physiotherapy ' were used A great range of methods is available but no indication of what combination of these was employed is given Moreover there is evidence in the paper that Dr Lawrence does not recognise the important influence of rest and tissue support to the joint in the earlier weeks of injection treatment

All the patients were male employees of the National Coal Board : so the analysis was by no means a measure of the results of treatment in a cross section of the community, and therefore cannot be accepted as a competent assessment It is well recognised that by the nature of his calling and perhaps by his psychological approach the miner is the most difficult of workmen to refit for work

Although the response to any form of treatment varies greatly in different joints no information is given on which joints were treated beyond the statement that the knees were most frequently affected the hips next' : in fact the analysis seems to be based on the treatment of a jumble of joints Nor is there any evidence that an attempt was made to correlate the degree of severity and loss of function with the radiological findings—loss of joint space, lipping bony deformity, and cyst formation

On the question of the technique of injection any penetration of a joint by a needle involves some trauma, but the finer the needle, the less the damage: unless aspiration is called for the needle should be of the finest calibre I use size — 19 hypodermic needles for the smaller joints and needles of 0 55 mm bore for the larger joints If wider needles are used the fluid will usually show some degree of hæmarthrosis

Dr Lawrence surprisingly says that "the accuracy of the injection was readily determined by injecting 1 c cm. of air with the solution, when the characteristic gurgling sound could be heard on subsequent movement of the joint.' Does he really require this pump handle technique to assure himself that he has reached the cavity of the joint ? It seems to be an entirely unsurgical and unjustifiable procedure: let him mix 5 ml. of lactic acid with 2 ml. of joint effusion and a spot of blood in a test tube, shake it up and note the frothy flocculent mess that results. The greatest care should be taken to avoid injecting air along with the solution

There are many other points that might be alluded to—e.g the number of cases that show excess of fluid in the joint (in knees, 1 in 5) or the doubtful value in osteo arthritis of raised plasma viscosity (any significant rise can usually be found to be due to some coincident condition, such as pulmonary tuberculosis, cystitis, or boils)

Professor Tait, who held a chair of natural philosophy, demonstrated that by the laws of physics, it was impossible to drive a "gutty" golf ball more than 150 yards whereupon his son, Freddie, who was amateur champion, drove his ball 182 yards his father's comment was that it only went to prove that no scientist should make a dogmatic statement without reviewing his premises meticulously, and being his own severest critic I venture to commend this dictum to Dr Lawrence, and to suggest that his final sentence should, for the present, read "It is concluded that among miners, and in my hands, lactic acid has no therapeutic action in osteo arthritis"

Sunderland W GRANT WAUGH

PREVENTION OF BARBITURATE POISONING

SIR —A note in your issue of Oct 24 draws attention to the production of barbiturate tablets made safe by the addition of ipecacuanha alkaloids The fact that these tablets are now available must be especially welcome to doctors called upon to treat patients suffering from melancholia Insomnia is an essential feature of the depressive psychoses, and must be effectively treated prior to, or in the early stages of, electroconvulsion therapy In the past, it has been customary to give such patients an adequate supply of one of the barbiturates This has usually entailed the issue of a large number of barbiturate tablets, but not without some misgivings in the mind of the doctor

In this connection, it was disturbing to read that a practitioner was censured for allowing the issue of 40 'Seconal' capsules to a depressed patient[1] It seems reasonable to suppose that these new barbiturate preparations could be prescribed for depressed patients without fear of criticism from any source In practice, these tablets are unlikely to check for long the efforts of the suicidal subject implacably bent on his own destruction However, they would serve to prevent accidental poisoning and perhaps to baulk purely impulsive attempts at suicide

The principle underlying the manufacture of the new ipecacuanha-barbiturate tablets might be employed in other ways For example, the addition of ipecacuanha alkaloids to preparations of 'Chlorodyne' might prevent addiction

Littlemore Hospital
near Oxford
J TODD

"CHEMOTHERAPEUTIC AGENT" AND "ANTIBIOTIC"

SIR,—The argument about the meaning of the word antibiotics must remind those with memories long enough of a similar argument about the word vitamins

Attempts to define vitamins have invariably failed, though Dr Leslie Harris probably came nearest to success (One recent definition is over eighty words long and contains the escape clause "as a rule" in its middle !) The reason for the failure is that each of the heterogeneous group of nutrients in question was in turn described as a vitamin by its discoverer, who did not stop to worry about definitions The word has a historical much more than a taxonomic significance Broadly speaking, all of the vitamins, at least all so far recognised, were discovered (or invented) between 1910 and 1950, some have fallen by the wayside—otherwise the number would be forbidding indeed

The analogy is even closer than at first might appear It is now generally recognised that a vitamin for one organism may not be a vitamin for another Is not precisely the same thing true of an antibiotic ? Provided we all know what we mean by antibiotics, does it really
matter whether chloramphenicol is or is not pu
the verbal pale merely because someone happens
synthesised it ? Supposing the synthesis (like
penicillin) had not proved to be commercially pr
and it had continued to be made by fermentatio
it have thereby retained the right to be called
biotic and have lost it merely because the
chemist and the chemical engineer successfully
synthesis on to the production plant ? It is rel
point out that ascorbic acid is still considered
vitamin though it has never been made commer
any route other than the synthetic The same
thiamine

I suggest that we continue to call antibioti
substances with the kind of property required,
by micro organisms (thus leaving out, for
purposes, any that may ultimately be extrac
higher plants), and discovered and investigate
the fourth decade of the 20th century and subse

London, N W 3 A L BACH

DEFECTIVE ANÆSTHETIC MACHIN

SIR,—On several occasions recently my atten
been drawn to a possible cause of failure with g
'Trilene' analgesia machines for obstetrics, an
seen no mention of this in any of the literatur
subject The fault may lie in the expiratory val

I first noticed this when I was offered a Fr
apparatus, and in testing it I found that no
trilene could be detected when it was used in the
manner Minnitt's apparatus was used instead, a
wards it was found that the expiratory valv
Freedman's apparatus had been taken to piece
enthusiastic midwife and put back upside dow
next time I had to teach analgesia to midwives I
to this, and then discovered that the expirato
parts on the Minnitt's apparatus provided w
pletely absent At a routine check in a maternity
it was found that the expiratory valves were def
half the machines

An expiratory valve must admit air drawn thr
machine during inspiration and no air throug
It must open easily on expiration If air enters
the valve on inspiration the machine is render
pletely useless This will occur if the spring fail
the small check-plate back on to its seating
failure may be due to rust on the spring, a slight
displacement of the disc, or tampering with t
parts and wrong replacement of them What
cause may be, failure to function properly is o
very easily brought about and is likely to pass u
unless expressly looked for I am convinced th
machines should never be used unless the user p
checks the expiratory valve in every case This
done by compressing the concertina tubing in
hand whilst one inspires through the face piece (
hygienically, through the metal fitting over w
face-piece is applied) If it is impossible to ins
valve is functioning correctly, but if inspiration is
the valve must be defective and it should be r
at once or another machine should be used

This policy, if consistently pursued, would n
avert complete failure in a large number of cases
a great deal of avoidable pain to women in lab
on many occasions the precaution will be ove
A far better plan would be for instrument manu
to construct a sturdier expiratory valve which w
less easily damaged by rust, trauma, or m
handling That the success of a scientific ins
should depend on the precise accuracy of a
check valve about half an inch in diameter, an
metal spring, seems unfortunate If the makers
apparatus could construct one that is proof ag
hazards they would do a great service

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[1] See *Lancet* 1953 i 1099

Meanwhile it behoves all who use these machines, and those who train midwives in their use and their care, to insist that the valve is *personally* checked before use in every case and that there are sufficient spare parts to make it possible instantly to replace one that is found to be defective.

St. Thomas's Hospital,
London, S.E.1
J D LAYCOCK

INCISION FOR ACUTE APPENDICITIS

SIR,—Appendicitis is the most important condition in general surgery and it is pleasing to see well informed support for the muscle splitting incision Mr E R Flint, of Leeds, taught me that it was the correct incision for appendicectomy, and seventeen years of emergency surgery has confirmed his opinion

The snag is to know which cases are appendicitis A very large number of them may be diagnosed with overwhelming probability clinically but I wish to draw attention to an old but neglected confirmatory method. If one does a careful abdominal and sometimes pelvic examination under relaxing anæsthesia most inflamed appendixes may be felt It is then a simple matter to make a small incision locate the cæcal attachment of the organ, detach it, and gently dissect it out from base to tip In dirty cases it is necessary only to close the peritoneum The muscles come together by themselves and the scar is inconspicuous if made in the line of skin tension In such cases the paramedian incision rarely gives any information not obtainable through the muscle-split It is a damaging incision and largely responsible for the run on surgical belts It is best reserved for doubtful case where investigation has failed to establish *any alternative diagnosis* In these cases the operation is more correctly termed exploratory laparotomy

Hull.
J CLAPHAM COATES

SIR,—In this correspondence all the old arguments in favour of the different incisions have been brought up again, as has happened for so many years and doubtless each surgeon remains satisfied with the incision he continues to use Mr Donald's advice last week is good. The soundness of each incision depends mainly on the care taken in opening and closing the abdomen

I hope that no-one will be led away by the last paragraph in last week's letter from Mr Downie. To use a Pfannenstiel incision for acute appendicitis (when it is difficult to be sure whether suppuration or perforation is present) is surely unsound surgery

London, W.1
JOHN HOSFORD

PERIODIC MEDICAL OVERHAUL

SIR,—If the value of periodic medical overhaul be equated with utility in spotting disease then abundant experience of the subject exists For my part I have done periodic overhauls for over twenty years: sick people, reputedly healthy nursery babies, and, more recently, school-children three yearly overhauls yearly overhauls, monthly and even weekly overhauls One has certainly had time to make up one's mind

Although these examinations have differed in bias, I recognise no essential difference in the basic technique of routine examination of sick men and men loosely believed to be healthy At the end one finds that periodic overhaul is chiefly of value *in detecting non lethal* conditions, in assessing progress and in getting some knowledge of the patient but it seldom reveals our first signs of major disease—of the disease for instance that eventually kills the patient This last phase involves "starting prices and disease has a nasty habit of starting between overhauls Furthermore, those of us who have seen some of the subjects of our overhauls in the post-mortem room can recall many mortifying instances of human fallibility in diagnosis. Thus (if my initial postulate be accepted) the value of periodic overhaul is definite but not extensive

It is of course open to some who adopt a different criterion of value to claim that the benefit conferred on one myopic by provision of spectacles makes endless effort worth while

An attempt to assess the value of periodic overhaul in the prevention of disease is appallingly difficult if we insist on separating observation from imagination Unhappily much that is written about the more ambitious extensions of the preventive ideal—health education and positive health—wears an air of detachment from reality In health education the more one departs from the simplest matters, the more one ceases to make sense *Again there is a world of wisdom in Sir Adolphe* Abrahams's doubt as to whether a medical man is the best person to give health education That particular doubt is at least as old as Plutarch [1] As for positive health I suspect it is a mysticism and speaking in all humility, I have but a very limited understanding of mysticisms.

Middlesbrough.
JOHN CAHILL.

CHILDREN IN HOSPITAL

SIR,—Premedication of children before operation *can* be done efficiently but it often is not Tonsillectomy is the commonest operation of childhood but in many hospitals the children receive no premedication at all (apart from atropine) because of a desire to have the child conscious and coughing immediately after operation To terrify a child, perhaps giving him lasting psychological symptoms for the sake of a non life saving operation seems to me to show a distorted sense of proportions Adults would not tolerate the treatment children get, although in their case the fear is far less since they realise that what is being done is for their own good

Mr Clarkson's statement (Oct. 31) that ' premedication of children is one of the most important unsolved problems in modern anæsthesia ' cannot be true. If it is unsolved it is *the* most important problem

Oxford
DAVID PYKE

SIR—As an ear nose, and throat surgeon I am sure Dr Mac Keith's article (Oct 24) will prove most helpful to a good many housemen and nurses when they have digested its contents

I cannot help feeling however, that some of the statements might lead to confusion on first reading particularly in the minds of readers without an intimate knowledge of modern surgical techniques.

I am thinking in particular of the reference to Levy [2] whose statement gives the impression that operations for tonsillectomy are commonly done before the age of 1 or 2 I cannot believe that many surgeons today are operating on patients of this age.

The other point in question arises in the discussion of How the Doctor Can Help Most surgeons nowadays insist on preoperative sedatives, except for relatively minor operations such as myringotomy Surely few hospitals can have returned to the days when a child was led personally by the doctor away from his mother straight into the operating room to have his tonsils out!

London, W 1
IAN G ROBIN

SIR,—*Dr Lucas (Oct 31) states that children should reach the anæsthetic room prior to surgery either fast asleep or in complete possession of their faculties "*

Often either because of the nature of the surgical emergency or because the operation is to be a brief one carried out in an outpatient, premedication is of necessity restricted to atropine Again in my last hospital the distance between the E N T wards and the operating theatres has made the use of 'Nembutal' inadvisable in children about to have tonsillectomy For these children I have found the following method of induction most satisfactory

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[1] Plutarch's Morals Part II. London 1684 p 106
[2] Levy D *Amer J Dis Child* 1945 69 7

If possible, the child is visited in the ward, the night before operation, and the anæsthetist then "makes friends" with him In an outpatient, this may have to be done in the few minutes preceding the induction. I tell the child that he is going to be told a story The great majority of children between the ages of 4 and 9 welcome this news Without saying anything about the anæsthetic, I then tell them a suitable fairy story or Rupert story After the first few sentences, the anæsthetic mask is placed about eight inches from the patient's head, and nitrous oxide allowed to flow at 10 litres per min. As the story progresses, so the mask is gradually brought a little closer to the face After about 5 minutes the child has usually lost consciousness, and it is possible to apply the mask to the face, and to add trichlorethylene, ether, or any other desired agent

Using this method, I found it possible to soothe most nervous children, and the great majority go to sleep without any sign of fear The only complaint has been that they did not hear the end of the story! Needless to say, this method of "premedication" is non toxic, and does not depress the reflexes It takes a little longer than other methods of induction, but I feel that the extra time spent is worth while

Alternatively, for children with visible veins, the technique of inducing with thiopentone, as described by Dr Bullough,[1] could hardly be improved With the use of a sharp needle, the child hardly feels the prick and goes to sleep quickly and safely

London, W C 1

ANDREW F FORBAT

SIR,—Following my letter in your issue of Nov 7 concerning the use of morphine in the postoperative treatment of children, I have had a request from a correspondent for further information concerning the formula I quoted—namely, age over age + 12 I would like to make it clear that this formula represents the fraction, according to the age of the child, of the official adult dose It does not represent the actual dose in grains

Black Notley Hospital
Braintree, Essex

M C WILKINSON

CORTISONE IN RHEUMATOID ARTHRITIS

SIR,—May I support strongly the sentiments expressed by Dr Copeman and Dr. Savage (Oct 17)? After an experience of twenty-five years in endocrinology, I looked upon the original claims for the therapeutic effects of cortisone and A C T.H with guarded optimism The present swing of the pendulum towards gloomy pessimism appears unwarranted, although not unusual The following case, of a patient known to Dr Savage and myself, illustrates the beneficial effect of small doses of cortisone in carefully selected patients even with a long history of rheumatoid arthritis, when other methods have failed completely

A woman, aged 51 (periods still regular), had a ten years' history of rheumatoid arthritis with moderate deformities of the fingers, wrists, knees, and ankles. In June, 1952 a recurrence began with swelling and pain, especially in ankles knees, and shoulders By August she could not leave her flat on the 2nd floor, because she could not manage the stairs. When seen by me in December, 1952, she was bedridden, immobilised and in continuous pain. Her erythrocyte sedimentation rate (E.S.R.) was between 68 and 80 mm (Westergren) after an hour Salicylates up to 12 g a day were without any effect, gold had caused untoward reactions in the past

By the end of February, 1953, she was receiving 25 mg of cortisone acetate daily with 3 g of (buffered) salicylates She has remained on that dosage to this day There was no dramatic change but a slow and steady improvement The pain has completely disappeared the deformities are the same as before the attack, but the swelling has gone Her appetite has become almost excessive, and she has stone in weight ; she now can manage 60 stairs and walk about 1 mile on the flat, slowly but fortably, and can do all the lighter housework cooking There have been no side-effects towards range and she appears mentally and

The story is the more remarkable, because for entirely personal reasons—could not be hospital, and biochemical examinations had to to a bare minimum Physiotherapy was given similarly restricted manner. The E.S.R. took over to decrease gradually to normal.

London, S W.3

V C

GOUT

SIR,—Dr Jennings's letter last week following questions

(1) Is interval therapy with gr 80 of sodium salicylate for 4 days per week sufficient to maintain the serum of gouty patients at a normal level, as has occur when gr 60–140 (usually gr. 90) of is given continuously ?

(2) Does interval therapy induce a favourable response in chronic gout, and if so, how does it that obtained by continuous therapy ?

(3) Does interval therapy induce loss continued therapy ?

(4) Should a high fluid intake be recommended ?

I suggest the following answers

(1) Dr Jennings's paper[2] stated "Our so far remained well as long as they have (sodium salicylate) in 80 gr doses daily for three or days a week Taken in this way it levels of blood uric acid" I take this to stopping salicylate therapy the serum uric acid return to abnormal levels within at least days Dr Jennings takes me to task for fact on a single patient, but I would perusal of the article will illustrate this point in and 6 which refer to 2 further patients. In my the serum uric acid almost invariably rises to levels within one to two days of stopping administration, even if this has been continued for months

It is unfortunate that Dr Jennings's paper did give sufficient serum uric acid figures to conclusions Bauer and Klemperer[3] were confirm them, and it appears that no such has ever been published

(2) Dr Jennings has presumably had interval therapy for at least sixteen of the many during which it has been advocated ment is often difficult to assess and it is not that, in the absence of really conclusive results therapy, there is divided opinion upon its degree It would appear that the subjective ment following continuous therapy, and detailed article under question, compares favourably published report with interval therapy

I would suggest that in those patients with radiological changes, repeated radiographs may objective evidence of response to therapy. It is significant that despite such considerable interval therapy there has not been a single radiological improvement, and yet within a few of continuous therapy it was possible to improvement in 3 patients[4]

(3) I find it difficult to believe that initial tration of sodium salicylate, in a dosage lower the serum uric acid appreciably, does not induce symptoms of salicylism. Graham[5] these symptoms were such as to make cinchophen a

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[1] Bullough J Lancet 1952, ii 999

[1] Marson F G W Quart J. Med 1953, 22, 331
[2] Rep chron rheum Dis 1937, 3, 106.
[3] Bauer W Klemperer F New Engl. J Med 1944, 231,
[4] Marson F G W Brit J Radiol. 1952, 25, 539
[5] Proc Roy Soc Med 1926, 20, 257

his retirement there was still no faltering, no hesitation. To onlookers he appeared to be almost nervously excited, but his steps were accurate, and the patient's recovery and convalescence were normally smooth A memory of the 'rag and bottle' days of anæsthesia was his constant attention to the patient's respiration Not only to a junior resident anæsthetist would he lift his head from his own work to ask 'Is she breathing ?', but also to an experienced honorary anæsthetist, sometimes to his obvious surprise and even annoyance! His regard for the well being of the patient on the theatre table had the disadvantage that it prevented him from delegating work to which his juniors felt entitled as part of their educational experience Feeling that the responsibility was his, he feared to relax it

'While Stevens was an outstanding teacher and a sound gynæcologist, perhaps he excelled as an obstetrician Not only was he skilled in the manipulations which were needed in those days, but he had an uncanny insight into the woman in labour He taught non interference whenever possible, for he claimed, and rightly, that most women in the real "travail" of the slow hours of inertia will deliver themselves without injury or distress of the fœtus if left alone under the influence of sedatives.

"All his friends and colleagues knew him as a genial companion, always interested in talk and fun There was a sparkle in his eye which was a gesture of welcome on meeting, and an answer to the talk of men He was never so happy as when a member of a little group round a table exchanging experiences and witticisms, reacting with his own infectious laugh and perhaps another story

"His chief recreation was fishing, at which he claimed the moderate success of all fishermen, and indoors he would devote something of his leisure to painting at which, as an amateur self taught artist, he excelled

"There was one thing he could not tolerate, and that was humbug, whether in the work of members of the profession or in his residents or students He was impatient of insincerity and prevarication, but honesty and straightness he was immediately sympathetic What he expected from those around him was the most impressive part of his own simple and honest self He was not a man of academic brilliance nor given to speculation in theory, for his thought was restrained in imagination He was an essentially practical man, wholly reliable, a model of the strictest professional honesty, and a warm and generous friend"

Mr Stevens married Lizzie Jane, the eldest daughter of the late John Reeves, of Blackheath, and she survives him Their son, Mr Russell Stevens, is a surgeon in Dorchester

CONSTANTIN LEVADITI

Constantin Levaditi, who died on Sept 5 this year, was born in 1874 at Galatz in Rumania. He began his medical studies at Bucharest and later worked in Rumania under Prof V Babès In 1898 he went to Paris to work with Albert Charrin in C J Bouchard's laboratory Soon afterwards he became a naturalised Frenchman Next he studied experimental medicine and pharmacodynamics in the Ehrlich Institute in 1900, and later in the same year he moved to the Pasteur Institute, where he worked first under Metchnikoff, then under Roux, and finally as *chef de service* In 1902 he published two books on *Contributions à l'étude des mastzellen et de la mastzellen-leucocytose* and *Le leucocyte et ses granulations* In 1905 he published one on *Antitoxische Prozesse* His attention was early drawn to skin diseases (which led to the publication of *Ectodermoses neurotropes* in 1922 and *L'herpès et le zona, ectodermoses neurotropes* in 1926, and to his being awarded the Cameron prize in 1928) and subsequently to syphilis, to which he devoted himself from 1905 for many years, paying particular attention to the *Treponema pallidum* Soon after Schaudinn had discovered the ætiological rôle of this organism, Levaditi demonstrated, on May 17, 1905, its presence in a newborn baby with congenital syphilis and thus proved that syphilis could be inherited In 1909, with J Roché, Levaditi published *La syphilis expérimentation, microbiologie, diagnostic* In collaboration with Pierre Marie, Levaditi showed that the antigen used in Wassermann's reaction was non-specific and could be superseded by normal liver and by ox heart, and with T Yamanouchi he showed that the antigen was a hepatic lipid With R Sazerac in 1921 he demonstrated the therapeutic effect of sodium tartrobismuthate in syphilis In 1923 he published *Die Prophylaxie der Syphilis*, and in 1924 *Le bismuth dans le traitement de la syphilis* With A. Navarro-Martin he discovered the antisyphilitic and prophylactic effects of oral treatment with derivatives of pentavalent arsenic, especially 'Stovarsol' with Ernest Fourneau In 1930 he published *Prophylaxie de la syphilis, prophylaxie locale, préservati per os, métalloprévention* Levaditi, however, is perhaps most famous for his method of staining the treponema of syphilis with silver (in 1906)

Much more recently, Levaditi examined antibiotics for antisyphilitic action after J F. Mahoney, in 1943, had discovered that of penicillin, and he also studied Nelson's reaction At every stage of the fight against syphilis Levaditi was to the fore, but he also investigated viruses and found in 1910, with Karl Landsteiner, that poliomyelitis was due to a filtrable virus. This led to his well-known work on the viruses of epidemic encephalitis, herpes, rabies, and the Coxsackie viruses, and the publication, in 1938, with Pierre Lépine and others, of *Les ultravirus des maladies humaines*, in 1948, with other workers, *Les ultravirus des maladies animales*, in 1945 his *Précis de virologie médicale*, in 1948 *La streptomycine et ses applications thérapeutiques*, in 1950 *Antibiotiques d'origine fongique, bactérienne ou végétale* and in 1951 *Le chloramphénicol et ses applications thérapeutiques*

All Levaditi's hypotheses were put to experimental test, and all his experiments on animals were strictly controlled histologically (in 1949 he published *Images électroniques en microbiologie*) He served in a medical capacity throughout the 1914–18 war In June, 1928, he was elected honorary member of the Académie de Médecine, in honour of which occasion Dr R. Mamet contributed to the *Vie Médicale* (1928, 9, p 779) a biographical note which unfortunately was mistaken in the U S A for an obituary notice, with the result that the *Surgeon-General's Index*, the *Cumulative Index Medicus*, Dorland's *Medical Dictionary*, and E C Kelly's *Encyclopedia of Medical Sources* antedated Levaditi's demise by a quarter of a century

Appointments

BARRETT JOAN M.R.C.S asst maternity and child welfare M.O. Durham County Council.

CLARK GWEN, M B Edin D OBST, D P H. asst county M.O. Worcestershire County Council

MAIR W G, M.B. Aberd. asst in the histological department The National Hospital Queen Square, London

PLEWS W R L.R.C.P.E D OBST, D P H. deputy M.O.H. and deputy port M.O Greenock

TEASDALE J M, B M. Oxfd appointed factory doctor, Retford, Nottinghamshire

The Hospital for Sick Children, Great Ormond Street, London

CAMPBELL, E D R, M A, B.M Oxfd part time registrar department of physical medicine

COYLE TERESA M.B N U I part-time senior registrar, ophthalmic department

HIGGINS R. N T, M B Camb part-time registrar department of psychological medicine

JEANES A. L M B Lond registrar, department of clinical pathology

MICHELL E P G, M B Camb M R C.P D C H house-physician department of child health.

SINGH S M M B Madras house-surgeon orthopædic and [illegible] departments

WALKER, C H M M D Edin. M.R.C.P.E, D C H senior medical registrar thoracic unit.

Leeds Regional Hospital Board

BEATON MURDOCH M D Edin. M.R C P E. consultant in general medicine Scarborough Bridlington, Malton, and Whitby groups

JORDAN J W, M D Lond, M R C P consultant in psychiatry and mental deficiency Hull and East Riding areas.

PHILPOTT M G, M.D Lond, M.R C P D C H consultant in pædiatrics Hull A Hull B and East Riding Groups.

REDMAN T F M.B Manc F R.C.S E., M R.C O G consultant in obstetrics and gynæcology St. James's Hospital and St. Mary's Hospital Leeds

ROBINSON L B M.B Leeds D C H asst. chest physician (S H M O) chest clinics and sanatoria, Hull area

SUMMERS G A C M B B.Sc Edin consultant in pathology City and County Hospitals York.

WOJCIECHOWSKI MIECZYSLAW, M B. Polish School of Medicine at Edinburgh asst anæsthetist (S H.M O), Dewsbury, Batley and Mirfield group

The British Social Biology Council (Tavistock House South, Tavistock Square, W C 1) express a somewhat austere attitude to Christmas in their photograph of a frozen lake in Buckinghamshire, but it is a good photograph, and the cards cost 6*s* 4*d* a dozen including envelopes and postage Some of their last year's cards (a photograph taken in the Forest of Fontainebleau) are also still to be had

The Grenfell Association (66, Victoria Street, London, S W 1) have carried on undefeatably their good medical work in Labrador and Northern Newfoundland Their well known cards include photographs and drawings of Labrador snow scenes, as well as several gently sentimental Christmas subjects Among these a new one, nicely designed by Betty Fyfe, shows an Eskimo child wrapped up to the nines, and a very young cherub in nothing but a nightshirt together decorating a Christmas tree out of doors on a cold night The cards are of different prices, ranging from 6*d* to 1*s* 9*d*, and are sold separately

A newcomer to this column is the National Spastics Society (44, Stratford Road, London, W 8) Their cards are in the old coach inn yard waits hunting lychgate tradition, and why not? A packet of 6 cards accompanied by six Christmas seals costs 2*s* 6*d* for the ordinary kind, or 4*s* for full colour reproductions with gold deckle edge and a ribbon. Perhaps when the society is a little older it will find an artist to express more personally its special good cause, but this is a start

PLAGUE OF FLIES

FOR the past few months swarms of flies have been causing much concern at seaside towns on the South Coast They have now been identified by the British Museum as two species of the genus cœlopa—*C frigida* and *C pilipes*[1] They usually prefer a warmer climate, but they have evidently been attracted by the great quantities of seaweed that have lately been washed ashore at several places on the South Coast These flies, which are black brown and bristly, are thought to breed exclusively in decaying seaweed, so it is hard to explain their recent appearance in London[2] They are attracted by certain smells, such as those of trichorethylene and chloroform, dry cleaners and chemists have reported troublesome invasions of their premises, though anæsthetists, it seems, have so far escaped There is disagreement among entomologists about the eating habits of these unpleasant creatures, but some say they are much addicted to beer Spraying with insecticides helps to keep down their numbers, but until the London plague is traced to its source it is unlikely that the flies will disappear Local authorities on the South Coast have decided to ask for Government help in dealing with the flies and the seaweed they thrive on

FAMILY PLANNING ASSOCIATION

THE second medical conference of the Family Planning Association was held in London on Nov 7

Dr M C Marwick and Dr E Wachtel described the technique and results of histological examination of material aspirated from the posterior fornix or scraped from the cervix with a wooden spatula As part of the routine of a birth control clinic, material has been collected in this way, spread on a glass slide fixed, stained, and forwarded to a cytological laboratory Malignant cells from various parts of the genital tract have been seen at a time when there was no clinical indication of disease, and also abnormal cells whose significance is not yet clear

Dr S M Dawkins said that in clinics the danger of the obviously infected patient was small compared with that of the symptomless carrier The major hazards of cross infection were not from instruments and caps which were always boiled, but from hands gloves, taps, soap bowls, and towels, and even from the tubes of the lubricating jelly used in some clinics Where antiseptics were used, care should be taken that these were suitable for the purpose and were used in the right concentration, and that the article was immersed long enough Plenty of soap and water was still one of the best antiseptics Dr Dawkins advocated the methods of cleansing and sterilisation described in the Medical Research Council's memorandum no 11 and war memorandum no 6

The meeting heard an account of the association's work in examining contraceptive devices submitted by manufacturers, and in issuing a list[3] of approved contraceptive creams whose spermicidal efficiency has been tested by bio assay

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[1] *Times* Nov 2 1953
[2] *Ibid* Nov 16 1953
[3] Obtainable from the association, 64 Sloane Street, London S W 1 1*s*

BRITISH MEDICAL STUDENTS' ASSOCIATION

THE annual general meeting of this association was held in Bristol on Nov 5, 6, and 7, and was attended by 5 delegates Prof G Gordon Lennon was inaugurated as his president

In a discussion on student health it was announced that the British Student Tuberculosis Foundation had provided tuition and convalescent care for 26 students suffering from tuberculosis, at its pilot centre at Pinewood, Berks There was also a waiting-list of 20 The foundation hopes to set up a larger, permanent centre A speaker pointed out that a student could be exempted, if he chose, from National Insurance contribution Even if he wished, however, he was unable to make any contribution other than as an unemployed person, and was thus debarred from any benefit if he fell ill

The next annual general meeting will be held in London in November, 1954

LEBANON HOSPITAL

FOUNDED in 1898, the Lebanon Hospital for Mental and Nervous Disorders at Asfuriyeh, Beirut, is still expanding; and in April this year a new treatment centre and nervous disorders unit was opened The hospital's report for 1952 shows that during the year 598 patients were admitted, and 575 discharged, and the daily average of patients in the hospital was 420 The number of applicants for the psychiatric nurses' training school, founded in 1948, is steadily increasing, and 16 first-year nurses were enrolled during the year The school has also launched a course for nurses who have graduated from various Middle East training schools in general nursing and who wish to take the Asfuriyeh certificate after one year of intensive training During the year the hospital received important additions to its staff In London, at the end of the year, Miss R Harvey became general secretary in succession to Miss Hilda Fox, who has retired after twenty seven years in this appointment

EXPERIMENTS ON ANIMALS

DURING 1952, according to the Home Office returns 2,117,912 experiments were made on living animals Of these 1,836 328 (86 6%) were made without anæsthetics. These experiments were mostly inoculations, modifications of the animals' environment or diet, or the administration of a drug or toxin The results of many of these experiments were negative and the animal suffered no harmful effects. Of the total experiments 95,901 were made in the course of cancer research, 202,435 for the purposes of public health or directly for the diagnosis of disease, and 810,676 for the standardisation of sera, vaccines, and drugs During the year 1348 visits mostly without previous notice, were paid by inspectors to registered laboratories The inspectors also visited 5 premises proposed for registration

TELEVISION AND THE FAMILY

THE Coventry Tutorial Class in Psychology, who reported last year on The Adolescent and Television,[3] have made a further investigation[4] this time into the impact of television on the family Their conclusions are so warmly in favour of this form of entertainment that it seems just possible that Mr Max Gordon, the tutor, and the engineer, the schoolmaster, the secretary, the education welfare officer, and the clerical officer who compose the group, are themselves keen televiewers They have, however, done their best to collect unbiased information by means of a questionnary distributed through primary and secondary schools situated in districts of the greatest possible variety The heads of the schools gave out the questionaries to children whose parents had a television set, telling them to ask their fathers to fill them up, if they were willing In this way, 1000 questionaries were distributed, and 250 were returned completed The group estimate that this represents a response from 1 in every 100 families with television sets in Coventry, and that it is a fair cross section

The first six questions (answered by the father in every case) asked how long the father had been a regular viewer, how long he had been married how many of his children lived at

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[1] The hospital's London offices are at Drayton House Gordon Street, London W C 1
[2] Experiments on Living Animals H M Stationery Office 1953 Pp 7 4*d*.
[3] *Lancet* 1952 ii, 1171
[4] Television and the Family Compiled by Max Gordon and published by the Coventry Tutorial Class in Psychology c/o 5, The Earl's Croft, Cheylesmore, Coventry, Warwickshire. Pp 20 2*s* 9*d*, postage paid

Royal College of Physicians of Ireland

The following have been admitted to the licence and membership

* Ghulam Bheck, C P Gore, R L McCorry, M. K O'Driscoll
* In absentia

The following have been admitted to the licence of medicine and midwifery

Adewale Omololu, Augustine Onyejiaku

Institute of Dermatology, London

A series of semi-permanent exhibitions is being shown at the institute during the winter course The third, from Dec 1 to 24, by Dr R W Riddell, will be on Mycology

Bust of James Bridie

A bronze bust of the late Dr O H Mavor (who wrote his plays under the name of James Bridie) has been presented to the University of Glasgow by his widow

Fulbright Travel Grants

The United States Educational Commission in the United Kingdom are offering these grants to citizens of the United Kingdom and Colonies who wish to visit America for study, research, or lecturing during 1954–55 The grants will cover the cost of direct travel between the candidate's home in the United Kingdom or Colonies and his destination in America, but since the funds of the commission are in non convertible sterling, it is not possible to offer grants for maintenance, tuition, or incidental expenses within the United States Further particulars may be had from the commission at 55, Upper Brook Street, London W 1

Diary of the Week

NOV 22 TO 28

Monday, 23rd

College of General Practitioners

5 45 P.M (Society of Apothecaries 14 Black Friars Lane E C 4) Dr Ian Watson Running of a Surgery and the Doctor's Round.

Postgraduate Medical School of London, Ducane Road W 12

4 P.M. Dr Raymond Daley Problems in Connection with Pulmonary Hypertension

Royal Society of Medicine, 1, Wimpole Street W 1

5 30 P.M *Section of Odontology* Dr J H Scott Growth of the Human Face

Institute of Neurology, National Hospital Queen Square, W C 1

5 P.M Prof. Paul Nayrac (France) Wilson's Disease

Medical Society of London 11 Chandos Street W 1

8 30 P.M Dr Robert Forbes Lessons from Recent Litigation against Registered Medical Practitioners

Manchester Medical Society

9 P.M (Clinical Sciences Building, York Place, Manchester) *Section of General Practice* Prof A M Boyd Senile Obliterative Arteritis of Legs (Film)

Tuesday, 24th

Royal College of Surgeons, Lincoln's Inn Fields W C 2

3 45 P.M. Dr L M Franks Benign Enlargement and Precancerous Hyperplasia in Human Prostate (Erasmus Wilson demonstration)

Society of Apothecaries Black Friars Lane, Queen Victoria Street, E C 4

4 P.M Prof J Henry Dible Pathology and the General Practitioner

5 15 P.M. Dr R. M B MacKenna Common Skin Diseases

British Postgraduate Medical Federation

5 30 P.M (London School of Hygiene and Tropical Medicine Keppel Street W C 1) Prof. H L Sheehan Vascular Lesions of Pituitary Necrosis.

Royal Society of Medicine

8 P.M. *Section of Medicine* Dr G E Beaumont, Prof. W Melville Arnott Prof C A. Wells Group-Captain C J S O Malley Use and Abuse of Rest as a Therapeutic Measure

Royal Eye Hospital, St. George's Circus S E 1

5 P.M Mr, T M. Tyrrell Management of Glaucoma

Institute of Dermatology, St John's Hospital, Lisle Street, W C 2

5 30 P.M Dr G B Dowling Tuberculosis of the Skin.

Institute of Obstetrics and Gynæcology

3 P.M. (Hammersmith Hospital, Ducane Road W 12) Prof. James Young Maternity in Great Britain.

West End Hospital for Nervous Diseases 40 Marylebone Lane, W 1

5 30 P.M Dr D Gordon When the Electro-encephalogram Helps

Liverpool Medical Institution 114, Mount Pleasant, Liverpool 3

8 P.M Prof G R Cameron, F.R.S. Liver as a Site and Source of Cancer (Florence Blair Bell lecture)

Wednesday, 25th

Postgraduate Medical School of London

2 P.M Prof C Rimington Porphyrin Metabolism.

Royal Institute of Public Health and Hygiene 28 Portland Place W 1

3 30 P.M. Dr H S Le Marquand Obesity in Children

Multiple Sclerosis Society

The inaugural meeting of this society, which has formed by a group of lay people most of whom have relatives suffering from the disease, is to be held at C Town Hall, London, S W 3, on Wednesday, Dec. 2, at 8 Further particulars may be had from the hon. secretary the society, 9, Grosvenor Crescent, S W 1

Society for the Study of Addiction

This society has chosen as the subject for the first H Norman prize (100 guineas) "the study or investigation substances, other than 'Antabuse' or its derivatives, distaste, disinclination, or dislike for alcohol." F particulars may be had from the editor of the *British J of Addiction*, 34, Addison Road, London, W 14 Contr should reach him not later than Dec 31, 1954

British Council for the Welfare of Spastics

A conference on the Cerebral Palsy Problem Today held at the London School of Hygiene and Tropical M Keppel Street, London, W C 1, on Saturday, Nov 10 15 A.M. The speakers will include Dr C D S. A Mr A Innes, Dr I M Holoran, and Dr E M Creak. T may be had from the secretary of the council, 28, Cr Parade, Limpsfield Road, Sanderstead, Surrey

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Prof Frederick Heaf is visiting Turkey and Greece, the auspices of the British Council, to lecture on tuberculosis.

The Pharmaceutical Society's calendar for 1953–54 has now published Copies (12*s* 0*d* plus 10*d*. postage) may be had from offices of the society 17, Bloomsbury Square, London, W C.1.

Institute of Dermatology

5 30 P.M Dr H Haber Cellular Nævi and Melanomata.

Institute of Obstetrics and Gynæcology

9 45 A.M (Chelsea Hospital for Women Dovehouse St S W 3) Miss A Bloomfield Pruritus Vulvæ.

Institute of Orthopædics

8 P.M. (234, Great Portland Street, W 1) Dr Angus Macphe Mr A W L Kessel, Mr G L W Bonney Disturbances in Poliomyelitis

Institute of Urology, 10, Henrietta Street, W C.2

5 P.M Mr Harland Rees Differential Diagnosis of Freq of Micturition

London Association of the Medical Women's Federation

8 30 P.M (Royal Free Hospital School of Medicine 8 H Street, Brunswick Square, W C 1) Mr C P Wi Vasomotor Catarrh

Birmingham Medical Institute, 154, Great Charles S Birmingham 3

8 P.M. *Section of Psychiatry* Dr J J O'Reilly Cr Responsibilities. (Presidential address.)

North Western Tuberculosis Society

5.30 P.M (Aintree Hospital, Liverpool 9) Mr Morriston Da Review of Treatment of Pulmonary Tuberculosis Future Prospects.

Thursday, 26th

British Postgraduate Medical Federation

5 30 P.M (London School of Hygiene and Tropical Me Dr H E Sigerist (Yale University) Science and H

Royal Army Medical College, Millbank, S W 1

5 P.M Mr James Laver, F.R.S.A Meaning of Military Un

Institute of Dermatology

5 30 P.M Dr R W Riddell Tinea Infections.

London Jewish Hospital Medical Society

8 30 P.M (11, Chandos Street W 1) Sir John Park Syncope

University of Oxford

8 30 P.M (Wingfield Morris Orthopædic Hospital.) Mr N Capener Evolution of Lateral Rachotomy

Liverpool Medical Institution

8 P.M Dr E P Hudson, Mr P P Rickham Emerge Newborn Infants

Honyman Gillespie Lecture

5 P.M. (University New Buildings, Teviot Place, Edinb Prof D M. Douglas, Prof I G W Hill Mitral in Relation to Surgical Treatment.

Friday, 27th

Postgraduate Medical School of London

4 P.M. Dr K Shirley Smith Clinical Features and Treatm Shock in Cardiac Infarction.

Royal Society of Medicine

5 P.M *Section of Pædiatrics* Prof J M. Smellie Dr C Hodson, Dr David Waterston Hiatus Hernia.

8 15 P.M *Section of Obstetrics and Gynæcology* Mr Harvey Fo Coöperation in Care of Carcinoma of Uterus. Mr Maxwell, Mr Donald Fraser Mr D M. Stern Rup Uterus in Pregnancy and Labour

Institute of Dermatology

5 30 P.M Dr I Muende Clinical demonstration.

Royal Institution of Great Britain, 21, Albemarle Stree

9 P.M Sir Alexander Fleming F.R.S. Antibiotics.

Medical Society for the Study of Venereal Dis 11 Chandos Street, W 1

7 30 P.M. Dr R R. Willcox, Mr A J King For and A Treatment Before Diagnosis.

Royal College of Physicians of Ireland

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ROYAL SOCIETY OF MEDICINE 1, Wimpole Street, W 1
5 30 P.M *Section of Odontology* Dr J H Scott Growth of the Human Face

INSTITUTE OF NEUROLOGY, National Hospital Queen Square W C 1
5 P M Prof Paul Nayrac (France) Wilson s Disease

MEDICAL SOCIETY OF LONDON 11 Chandos Street W 1
8 30 P.M Dr Robert Forbes Lessons from Recent Litigation against Registered Medical Practitioners

MANCHESTER MEDICAL SOCIETY
9 P M. (Clinical Sciences Building York Place Manchester) *Section of General Practice* Prof A M. Boyd Senile Obliterative Arteritis of Legs (Film)

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5 30 P M (London School of Hygiene and Tropical Medicine Keppel Street W C 1) Prof H L Sheehan Vascular Lesions of Pituitary Necrosis

ROYAL SOCIETY OF MEDICINE
8 P.M *Section of Medicine* Dr G E Beaumont Prof W Melville Arnott Prof C A. Wells Group-Captain C J S O'Malley Use and Abuse of Rest as a Therapeutic Measure

ROYAL EYE HOSPITAL, St. George s Circus S E 1
5 P.M. Mr. T M. Tyrrell Management of Glaucoma

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Mr A W L Kessel Mr G L W Bonney,
Disturbances in Poliomyelitis

INSTITUTE OF UROLOGY, 10 Henrietta Street, W C 2
5 P.M Mr Harland Rees Differential Diagnosis of Fr
of Micturition

LONDON ASSOCIATION OF THE MEDICAL WOMEN'S FEDERAT
8 30 P M. (Royal Free Hospital School of Medicine 8 I
Street, Brunswick Square W C 1) Mr C. P
Vasomotor Catarrh

BIRMINGHAM MEDICAL INSTITUTE, 154, Great Charles S
Birmingham 3
8 P.M. *Section of Psychiatry* Dr J J O Reilly C
Responsibilities (Presidential address)

NORTH WESTERN TUBERCULOSIS SOCIETY
5 30 P M (Aintree Hospital Liverpool 9) Mr Morriston D
Review of Treatment of Pulmonary Tubercul
Future Prospects.

Thursday, 26th

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropic
Dr H E Sigerist (Yale University) Science

ROYAL ARMY MEDICAL COLLEGE Millbank, S W 1
5 P.M Mr James Laver F R.S A Meaning of Militar

INSTITUTE OF DERMATOLOGY
5 30 P M Dr R W Riddell Tinea Infections

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8 30 P M (11, Chandos Street W 1) Sir John P
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UNIVERSITY OF OXFORD
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LIVERPOOL MEDICAL INSTITUTION
8 P.M Dr F P Hudson, Mr P P Rickham Emerg
Newborn Infants

HONYMAN GILLESPIE LECTURE
5 P.M (University New Buildings Teviot Place, Edin
Prof D M Douglas Prof I G W Hill Mitral
in Relation to Surgical Treatment.

Friday, 27th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P M Dr K Shirley Smith Clinical Features and
Shock in Cardiac Infarction

ROYAL SOCIETY OF MEDICINE
5 P M *Section of Pædiatrics* Prof J M. Smellie
Hodson Dr David Waterston Hiatus Herni
8 15 P M *Section of Obstetrics and Gynæcology* Mr Ha
Coöperation in Care of Carcinoma of Uterus
Maxwell, Mr Donald Fraser Mr D M. Stern
Uterus in Pregnancy and Labour

INSTITUTE OF DERMATOLOGY
5 30 P M Dr I Muende Clinical demonstration.

ROYAL INSTITUTION OF GREAT BRITAIN 21, Albemarle St
9 P M Sir Alexander Fleming, F R S Antibiotics.

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL D
11 Chandos Street, W 1
7 30 P.M Dr R. R. Willcox Mr A. J King - For and
Treatment Before Diagnosis

Clearly in neurology, as in other specialties, some of the day-to day work must be done by those who have not the specialist's special training, but it is the task of the clinical neurologist to maintain standards, and by teaching and personal contacts to make his colleagues aware of developments in his particular field, so that not only is their own work more discriminating but they become increasingly able to recognise when his help would be valuable Consequently the need for the clinical neurologist in the ordinary practice of medicine has never been so great as it is today

Research

Now I turn to the prospects of research in clinical neurology In the development of new ideas the relationship between observation and hypothesis is an intimate one, for not only do observations suggest a new hypothesis, but often a new hypothesis points to fruitful new observations In this sphere, also, it would be artificial to distinguish clinical observations from those made by other methods, and in the sphere of research the number and variety of such ancillary observations is considerably greater than in neurological diagnosis, because it includes animal experiments Up to the end of last century the great clinical neurologists were limited in constructing their hypotheses to correlating their clinical observations with the lesions revealed by pathology and with the very limited knowledge of neurophysiology then available The work of such a man as Hughlings Jackson illustrates what rich and fruitful ideas the mind of a genius could evolve from these limited types of observation, and I believe that what I may perhaps call the Jacksonian method is still rich in possibilities

Much work remains to be done in the sphere of aphasia and in the interpretation of those perceptual disorders which impair the recognition of objects, and the awareness of space and of the body Our knowledge of these subjects has been greatly enriched during recent years by many new observations, but in considering these difficult questions we need perhaps fresh unifying concepts which will enable us to see some common pattern of disordered function underlying disorders of thought, speech, and recognition, and also will clarify the idea of cerebral localisation Here the neurologist has a unique contribution to make to the illumination of the brain-mind relationship

Today, indeed, there is no sharp distinction between neurology and psychiatry, for they share an interest in the neurological basis of all aspects of mind. We recognise this overlap alike in our daily practice and in the great contributions which neurology has made to psychiatric therapeutics I believe that the fertility of the marriage between the two specialties is far from exhausted

FRESH TECHNIQUES OF OBSERVATION

Now let us turn to the new avenues for research which have been opened by the fresh techniques of observation which have been developed during the present century and, more particularly, during the last twenty five years Two of the most impressive of these, of course, are electro encephalography and the various forms of neuroradiology It seems to me that the great advances so far made by electro-encephalography have been even more important for theory than for practice, and this is true especially of neurophysiology If we look at the recent development in our knowledge of epilepsy, it is fascinating to see how clinical observation, clinical electro-encephalography, and neurophysiological electro-encephalography have blended to give us already the outline of a conception of a central mechanism regulating consciousness. This is [illegible] by the observations of Penfield on highest [illegible] the work of Magoun and his colleagues on [illegible] reticular activating system and that of Jasper and Droogleever-Fortuyn on the experim production of a petit-mal type of dysrhythmia. B should be noted that it is clinical neurology provides the inspiration for this work, for it is in alone that the psychological content of highest seizures can be studied and it is in man that petit can best be observed Consequently it is only in as the clinical neurologist by his observations is ab differentiate different types of epileptic attack th provides the material for the construction of hypot to which the observations of the electro-encephalogr and the neurophysiologist contribute

There are two further fruitful developments of researches The hypothesis of the rôle of the ce reticular formation in the control of consciousness application in the clinical study and differentiati prolonged disturbances of consciousness—i.e., stat stupor and coma, to which some neurosurgeons example, Cairns, Jefferson, and Obrador, have particular attention Abnormal states of sleep, drea and the hallucinoses constitute a closely related fi study, and in the experimental investigation of the of action of the hallucinogenic drugs neurology, ps logy, electro encephalography, and pharmacology hands with psychiatry in a piece of work which not is of great intrinsic interest, but may throw valuable upon the symptomatology of the psychoses, partic schizophrenia

BIOCHEMISTRY OF THE NERVOUS SYSTEM

Finally, I come to a field which, at first sight, may more remote from clinical neurology than those which I have so far touched, I mean the biocher Cajal, you will remember, in the passage I have al quoted, sought as an ultimate scientific objectiv physico chemical representation of events The litt have already learnt about the biochemistry of nervous system has been enough to show the impor of this subject in the interpretation of all neurol phenomena The biochemistry of the vitamins o B group has revealed something of the complexity o intracellular enzyme processes in the nervous sys and, after all, all pathological changes are fundamen physico-chemical changes Hence the biochemistr the nerve cell enters not only into those disorders w are commonly called metabolic, but also into its rea to infections and the processes of resistance and im nity, into the care of the comatose patient, the dea survival of cells after vascular occlusion, and the degenerations which are either hereditary in orig associated with the process of ageing If we add to t the biochemistry of the synapse, whether within nervous system itself or in the autonomic ganglia, o myoneural junction, and of the metabolism of muscles themselves, the significance of biochemistry neurology needs no emphasis

What I would emphasise, however, is the part t played by the clinical neurologist in the biochem field. It is not often that he will himself be an ex biochemist, but he must surely be sufficiently in t with what is going on in the biochemistry of the ner system, not merely to work in fruitful collaboration the biochemist, but to be able to suggest to his biochem colleagues promising fields of research Biochem research in neurology always begins either because clinical neurologist asks the biochemist a question because he presents the facts of clinical neurology to biochemist in such a way that the biochemist him asks the question

Take myasthenia as an example The discovery of value of physostigmine and all the knowledge that flowed from it was based upon a clinical observat The thymus was brought into the picture by the pat st, but only because he discovered abnormalities in thymus in patients already labelled as suffering from sthenia by the clinician. From this sprang thymec y and the observations of pharmacologists and iologists on a possible relationship between the mus gland and the myoneural junction Essential ugh the contributions of the non-clinical scientists are he solution of the problem, I do not believe that the k of the clinical neurologist is therefore finished king broadly at the clinical picture he may well ask self whether myasthenia is a single entity—whether act it is a disease or a symptom, whether there is h a thing as thyrotoxic myasthenia as well as an ciation between thyrotoxicosis and myasthenia vis, and where in the picture are to be placed the sthenic syndromes associated with avitaminosis and h carcinoma of the lung In other words the contri ons which the pathologist and the biochemist are king to the building up of the hypothesis about sthenia should stimulate the clinician to discriminate ther in his own field.

nd so one might multiply instances the various ms of polyneuritis, motor neurone disease, dissemi ed sclerosis, parkinsonism of the degenerative type, n epilepsy itself at once suggest themselves as fields research where the clinical neurologist with a wledge of the possibilities of biochemistry may e a contribution which he alone has the power to ke.

The relationship between the metabolism of the vous system and that of the rest of the body is still ost uncharted territory How rich it is in possibilities hown by recent research on the metabolism of copper d the amino-acids in Wilson's disease, and this also ws how important are the links between neurology d internal medicine.

A Challenge

I have but touched the fringe of a vast subject, but hope I have said enough to convince you that the spects for clinical neurology were never brighter than y are today Let me conclude with some words of ful which are both an encouragement and a challenge s, his successors:

"Great men are at times geniuses, occasionally children, t always incomplete. Even granting that the genius jected to the test of critical inspection emerges free from error we should consider that everything that he has covered in a given domain is almost nothing in comparison th what is left to be discovered. Nature offers to all of us xhaustible wealth, and we have no cause to envy those who ceded us, nor to exclaim as did Alexander in consequence the victories of Philip: My father is going to leave me thing to conquer!"

The long words of science are justified because they unfamiliar This seems to be a doubtful recommendation d one which suggests that the scientist takes a pride in ning pages that are deliberately obscure. This is not so e apparent unfamiliarity of scientific words, the air they are of belonging to a specialised type of thought and language, ts them apart, in some way from the speech of everyday e. This is an advantage to the users of both languages. tepless and amorphous are literally the same sleeplessness es not seem to be very different from insomnia, yet in each e both words have their appropriate uses, and the English nguage is the richer because both are available It is not ue to say that either language can be translated into or placed by the other without loss. The loss may be small, d hypogeal is replaced by underground it is much greater if ypostatic is translated into understanding It may even be complete. Kipling once told us that,

> The Colonel's Lady an' Judy O'Grady
> Are sisters under their skins.

His meaning is lost if a scientist describes them as subcutaneous siblings."—T H. Savory *The Language of Science*. London, 1953, p. 184.

CORONARY HEART-DISEASE AND PHYSICAL ACTIVITY OF WORK

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(*Concluded from p 1057*)

II STATEMENT AND TESTING OF PROVISIONAL HYPOTHESIS

The suggestion emerged from part I of this paper that physical activity in work is associated with a lower incidence and severity of coronary (ischæmic) heart-disease in middle-aged men This proposition is interesting in view of the present dearth of useful theories on the causes of coronary heart-disease and of its probable increase The possibility that the association may be a causal one, and that factors of *low* incidence and mortality may be identified in occupation, is worth pursuing in the hope of eventually discovering clues to the prevention of the disease. As has so often happened in epidemiology clues may be discovered before the intimate processes of the disease are fully understood. We therefore adopted the suggestion as a working hypothesis, and proceeded to test it as best we could. The provisional hypothesis may be stated, as an association between variables, thus:

> Men in physically active jobs have a lower incidence of coronary heart-disease in middle age than have men in physically inactive jobs. More important, the disease is not so severe in physically active workers, tending to present first in them as angina pectoris and other relatively benign forms, and to have a smaller early case-fatality and a lower early mortality rate.

Since there was no indication that the greater incidence and severity of coronary heart-disease in the physically less active workers was associated particularly with mental factors in their work and for other reasons, no alternative hypotheses were framed for the present in psychological terms and the observations were confined as far as possible to the dimension of physical activity and inactivity of work The hypothesis, thus is not advanced in any exclusive sense it was necessary, however to try to isolate it if any progress was to be made.

Methods Adopted in Testing the Hypothesis

In this type of research dealing as it often must with material impossible to control," of less accuracy than might be wished and from which it is difficult to isolate variables, *special precautions need to be taken by the investigator* In the present instance reliance was placed on the power of simultaneous attack on the problem from different directions and independent bodies of material were used so that the cumulative effect (as well as individual findings that may by themselves lack conviction) can be considered

Attempts have been made to test the provisional hypothesis by observing its capacity to predict in a variety of situations. The following tests were carried out

First test.—Enlarging the evidence by a further period of observation of the experience from which the original observation was made (London Transport and the Post Office)

Second test.—Extending the hypothesis from early to all coronary mortality and observing the national experience

TABLE VII—MORTALITY IN FIRST 3 MONTHS OF FIRST CLINICAL EPISODE OF CORONARY HEART DISEASE DRIVERS AND MALE CONDUCTORS (AGED 35–64 INCLUSIVE) OF CENTRAL BUSES OF LONDON TRANSPORT EXECUTIVE, 1949-5

Average Annual Rates per 1000

TABLE VII(A)
1951–52

Ages (years)	Early mortality (first 3 months)	
	Drivers	Conductors
35–44	*0 5*	
45–54	*1 0*	
55–64	*4 0*	*2 3*
Total no of deaths	32	9
Standardised rate at ages 35–64 incl.	*1·5*	*0 8*

TABLE VII(B)
1949–52

Drivers						Conductors					
Ages (years)	Man-years observed	Immediate mortality (first 3 days)	Mortality at 4 days to 3 months	Early mortality (first 3 months)		Ages (years)	Man years observed	Immediate mortality (first 3 days)	Mortality at 4 days to 3 months	Early mortality (first 3 months)	
				No of deaths	*Rate per 1000 p a.*					No. of deaths	[illegible]
35–44	15,878	*0 3*		6	*0 4*	35–44	13,510			2	
45–54	17,188	*0 8*	*0 4*	20	*1 2*	45–54	7606	*0 5*		4	[illegible]
55–64	9814	*2 6*	*1 2*	37	*3 8*	55–64	5300	*1 1*	*1 1*	19	[illegible]
Total no of deaths		44	19	63		Total no of deaths		12	6	18	
Standardised rate at ages 35–64 incl		*1 1*	*0 5*		*1 5*	*Standardised rate* at ages 35–64 incl.		*0 5*	*0 3*		[illegible]

Definitions as in tables I and IV

Further population counts were made as on Jan 1, 1952 and 1953

0 001 < P < 0 01 testing the difference in table VII(B) between drivers and conductors both in immediate mortality and early mortal using the t test.

of twenty years ago, described in the Registrar General's Occupational Mortality Supplement

Third test—Making deductions from the hypothesis in terms of the course of coronary heart disease as well as its incidence and mode of presentation, and trying to verify these on yet another set of data—a current sample of death certificates

First Test (Direct Confirmation) Further Observation of Transport and Postal Workers

The information in part I covers the years 1949–50, and it was mostly collected by the middle of 1951 The analysis, however, could not be undertaken until 1952, and by this time it was impracticable to collect detailed morbidity data for 1951 and 1952, highly desirable though this was now seen to be The deaths, however, that occurred during those years were recorded in the Central Record of Staff Statistics of London Transport Executive, and the Post Office has for many years kept records of the mortality of its staff Since the lower death-rates of the conductors and postmen during the first days and weeks of clinical coronary heart-disease were the main findings in 1949–50 it was clearly important to know whether these workers maintained their advantage in 1951–52, particularly since wide variations in mortality-rates from year to year are commonly found in this type of study even when dealing with substantially larger numbers of cases than we have been able to do

Table VII(A) gives the early mortality rates from coronary heart-disease among the drivers and conductors of the central ("red") buses in 1951–52 (The figures for tram and trolleybus drivers and conductors are not shown in table VII because the trams were being withdrawn during 1951) The drivers have a higher mortality in each ten-year age group during 1951–52 (in each five year group also) and the standardised rate summarises the excess as 90% This was little different from the findings in 1949–50, the greater excess shown in the middle columns of table IV being mainly due to the particularly low mortality among the tram and trolleybus conductors

Table VII(B) amalgamates the experience of the central bus workers for the four years by adding and averaging the deaths and population figures over 1949–52 The 'immediate mortality" of the drivers is seen to be about twice that of the conductors, and mortality in the rest of the first three months is about two thirds higher, total early mortality is over 80% as much again in the drivers as in the conductors

Table VIII(A) describes the early mortality among the five postal grades during 1951–52 The Civil Service executives and clerks were not studied in 1951–52, so, unfortunatel only one truly sedentary grade remains—the telephon In 1951–52, as in 1949–50, the postmen had a substanti lower early mortality than the telephonists, comparis with the three "intermediate" grades are again of lit interest The combined rate for 1949–52 in table VIII(B) sho the by now expected trend (fig 2)

Summing up in 1951–52 the physically more acti workers (conductors and postmen) had lower ear mortality-rates than the physically less active worke (drivers and telephonists, respectively) Enlargeme of the evidence by two further years' experience therefor supports the hypothesis

The next test should be to repeat these special observa tions in different groups of workers, but this would me

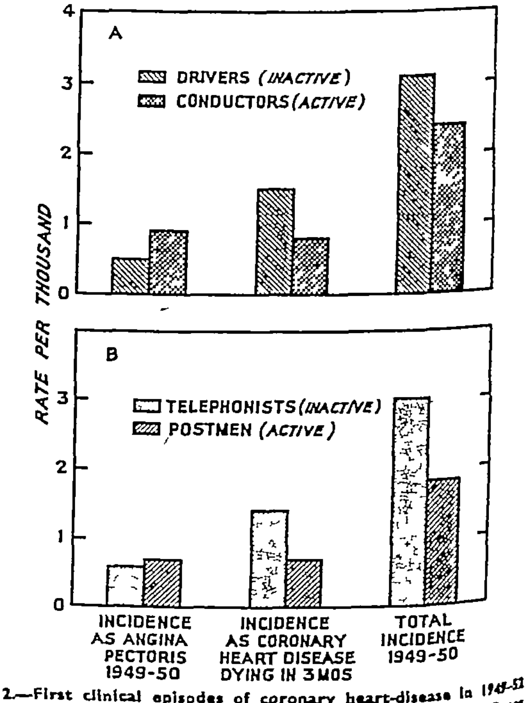

Fig 2.—First clinical episodes of coronary heart-disease in 1949-51: A, drivers and male conductors, aged 35–64, of Central London Buses, B G P O male telephonists and postmen, aged 35–59

lay of some years before results could be available therefore turned to data already available, such having the merits and drawbacks of being collected quite other purposes.(c)

ond Test Physical Activity of Work, and the Death rate from Coronary Heart disease

has been postulated, as the most important part he hypothesis to be tested, that the "early mortality" coronary heart-disease—death in the first three ths of the clinical disease—is lower in middle-aged in physically active jobs than in men doing physically tive work. But it has previously been suggested his series[14] that this early mortality is responsible about three-quarters of the coronary deaths in ddle age.(d) The present postulate may thus be ended to include *all* coronary deaths

That men doing physically active work have a lower mortality from coronary heart-disease in middle age than men in less active work.

test of this extended hypothesis will be a test though rhaps not a rigorous one, of the original hypothesis. It was decided therefore to make a special analysis the mortality from coronary heart-disease in the rious occupations for which data are available in the gistrar-General's Occupational Mortality Volume of e Decennial Supplement for 1930–32[17] the latest nd only) years that could be studied "Coronary rombosis" was beginning to be commonly diagnosed this country late in the 1920s,[18] so the analysis is making

LE VIII—MORTALITY IN FIRST 3 MONTHS OF FIRST CLINICAL ISODE OF CORONARY HEART DISEASE IN MALE POSTAL ORKERS (AGED 35–59 INCLUSIVE) 1949–52

Standardised Rates per 1000 per Annum

Occupation	TABLE VIII(A) 1951–52 Early mortality (first 3 months)		TABLE VIII(B) 1949–52 Man years observed	Early mortality (first 3 months)	
	No of deaths	*Rate per 1000 p.a.*		No of deaths	*Rate per 1000 p.a.*
tmen	68	*0·7*	160 986	125	*0·7*
tal and telegraph officers pervisors lmen higher grade	51	*1·8*	57 440	104	*1·8*
lephonists	16	*1·6*	25 144	29	*1·4*

Definitions as in tables I, IV and VI
Further population counts were made as on Jan. 1 1953

METHOD

It is very difficult to differentiate between the occupational oups of social class I (the leading professions managers, ners, &c.) or of social class II ("lesser" professions, &c.) terms of the physical work they involve. We therefore amined social classes III (skilled workers) IV (semi-skilled rkers), and V (unskilled workers) which include a wide riety of heavy and light jobs. There are mortality data for occupational "groups" in these three classes (excluding e Armed Forces) and they contain over 2½ million men ed 45–64 years—the great majority of all the men in these sses.

They used three categories:

Categories	Groups	No of men
A Physically heavy jobs	16	670 465
B Physically light jobs	23	546 012
C Intermediate and doubtful jobs—i.e., jobs which were both heavy and light or neither; about which the referees disagreed or which they were unable to to classify	31	1 400 549
Total	70	2 617 026

(The contents of the categories are detailed elsewhere[19]) We then sorted the groups into their social classes, and calculated death rates for coronary heart-disease.

We do not in our unit have the necessary knowledge to make an informed grading of these occupation groups to heavy and light work, especially for as long ago as 1930–32. And for a different reason, also we invited others to make the classification for us It is important in this kind of inquiry to take precautions against any recognisable source of "bias": in the present instance the grading of jobs should obviously be "blind," so that in cases of doubt the decision whether a job is heavy or light in respect of physical activity cannot be affected by knowledge of what is happening to the other variable being studied—coronary mortality We therefore requested two colleagues, experts in industrial medicine to classify the occupation groups—without telling them our hypothesis or indeed, what problem we were investigating They kindly agreed and, in addition, they did the grading independently consulting together only at the end over a few doubtful groups.

TABLE IX—MORTALITY FROM CORONARY HEART-DISEASE IN HEAVY AND LIGHT WORKERS (MEN AGED 45–54) ENGLAND AND WALES, 1930–32

Average Annual Death-rates per 1,000 000

Social class	Physical demands of work		
	Heavy	Intermediate and doubtful	Light
III	*172*	*225*	*341*
IV	*168*	*158*	*327*
V	*87*	*236*	*323*
Mixed	*78*		*265*
Total classes III IV and V	*139*	*239*	*337*
Total no of deaths (3 years)	154	531	321
1931 Census population ×3	1 110,390	2,303 772	951 732
Men Aged 55–64			
III	*497*	*608*	*916*
IV	*353*	*468*	*556*
V	*363*	*490*	*738*
Mixed	*259*		*561*
Total classes III, IV and V	*396*	*530*	*866*
Total no. of deaths (3 years)	357	983	519
1931 Census population ×3	901 006	1 855 675	668,304

Death-rates calculated from information given in table 4A of the Registrar-General's Decennial Supplement, part IIa (1938).[17]
Deaths are those certified to no 94 of the Fourth Revision of the *International List of Causes of Death*, 1929
The classification of occupation groups was specially made.

The rates for classes III IV and V combined at other ages were:

Ages (years)	Heavy	Intermediate and doubtful	Light
35–44	*46*	*61*	*61*
65–69	*859*	*1137*	*1745*
70–74	*13 7*	*1501*	*2307*

(c) The first two authors alone are responsible for the remainder of this paper

(d) This study[14] showed that 70% of all coronary *deaths* during the years 1940–50 among a group of medical practitioners, aged 40–64, took place in the first month of the first clinical attack of the disease; the majority of these being deaths in the first few days (here called "immediate").

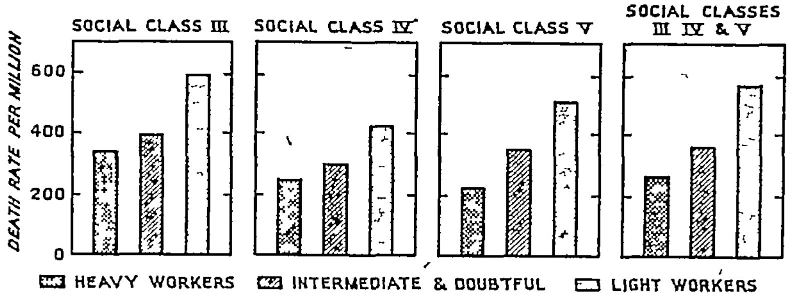

Fig 3—Mortality from coronary heart-disease in heavy and light workers, men aged 45–64, in England and Wales in 1930–32.

RESULTS

The results are shown in table IX and summarised in fig 3. In brief, the coronary mortality of the groups doing physically heavy work is rather less than half that of the light groups. The advantage of the heavy workers is seen at ages 45–54 and 55–64 separately, and in the social classes individually. As satisfactory (technically speaking!) as this finding, which supports the hypothesis, is the central placing of the intermediate and doubtful groups, and the strong "trend" shown in the figures. Moreover, the fact that the excess mortality of the light occupation groups is no more evident among the skilled men of social class III than in the semi skilled workers of social class IV and the unskilled workers of class V does not suggest that there is an important psychological strain involved in the light occupations which might be responsible for *their* excess mortality. These jobs in classes IV and V—skilled workers in gas works service, metal machinists, metal glazers, &c., barmen, printing-machine minders, printers, &c., messengers and porters (excluding railway, &c., porters)—do not obviously involve "responsibility" or special "brainwork," however much some light jobs of social class III may or may not be saturated with psychological stress factors. Fig 4 plots the mortality rates of occupation groups with an average of 10 or more deaths per year, and shows almost no overlap of heavy and light groups. If there is a major psychological influence operating to produce the mortality gradient of table IX, the scatter of fig 4 suggests that it is so intimately associated with the physical factor as not to be readily distinguishable from it.

DISCUSSION

The validity of this test depends on several things, including the classification of the occupations. We cannot at the moment do anything about that. Of another order is the difficulty which arises because men may change their jobs on account of illness. They may be advised, for instance, to transfer from heavy work to light for the sake of their health, and the mortality-rates in light jobs may thus be exaggerated. (Certain low skilled light jobs indeed are often reserved for the infirm.) This is one disadvantage of having to accept the last occupation before death as a sufficient indicator of a man's main occupation during his life. As already indicated, however, this problem is unlikely to be critical in the present instance, because a majority of all deaths from coronary disease in middle aged men probably occurs in the first clinical episode of the disease—i e, *before* there is opportunity to change jobs on account of it. The distribution of deaths in the doctors has already been mentioned. The standard of diagnosis in these doctors is likely to be particularly high, and premonitory clinical manifestations of coronary heart-disease, mild or atypical as well as typical, are far likelier to have been diagnosed among them in 1940–50 than in the general population in 1930–32. Yet, as has been said, in almost three quarters of the coronary deaths among the doctors there was no record of illness (lasting as much as a week) due to coronary heart disease before the first reported and fatal attack.

Two further pieces of evidence may be mentioned in support of this proposition.

(1) In a representative sample of death certificates obtained for another inquiry and referring to March, 1952, there were, in men aged 45–74 years, 118 deaths from coronary heart-disease about which some clinical information was available. From this information it appeared that 83 (70%) of the deaths had probably occurred in first clinical episodes of the disease, and 35 probably in second or later episodes. This material will be discussed more fully in the next test of the hypothesis.

(2) A group of light occupations which are highly specialised and require considerable skill and training was isolated from social class III in the Registrar-General's occupational mortality data. Such occupations are potter, compositor, french polisher, railway engine driver, railway signalman, and the police. It is very unlikely that middle aged men will transfer to these occupations because they are suffering from coronary heart-disease, or one of its precursors (or even from ill health not considered at the time to be related to coronary heart-

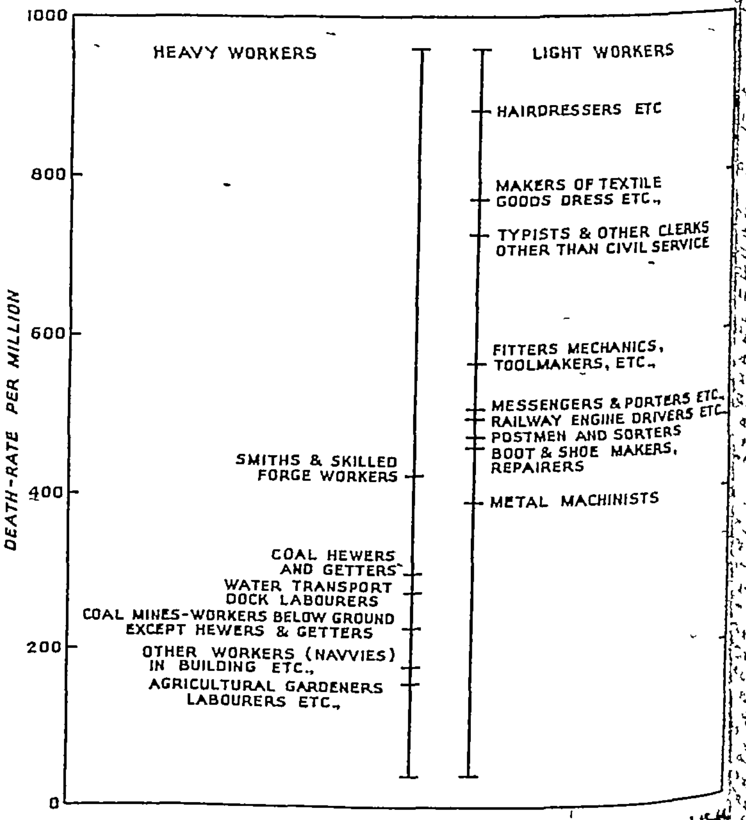

Fig 4—Mortality from coronary heart-disease in heavy and light workers men aged 45–64 in England and Wales in 1930–32. Rates for occupation groups in social classes III, IV and V having 10 or more deaths per year

ae). Moreover certain of these occupations will require -employment medical examination The mortality from ary *heart disease* in this *special* group of light occupa was found to be substantially greater than in the heavy ers of social class III, and this excess was apparent from 4 through 70–74 years of age. This is evidence of course about one side of the problem—that light workers have h mortality

he only alternative explanation we can think of which it account for the trend of table IX is that since y workers live often in villages and small towns light workers in cities where medical facilities have been better the diagnosis of coronary heart se—still a relatively 'new' condition in 1930–32— ht have been more readily made in light workers vever in the years under consideration, mortality as commonly ascribed to so-called myocardial e in light workers as in heavy workers, and this ers unlikely an explanation depending mainly on the ity of diagnosis and certification It will be interest to observe the trends of occupational mortality een 1930–32 and 1949–53 when figures for these er years become available and this may provide ther test of the hypothesis (The suggestion from the minary figures for 1949[10] is that the difference een heavy and light workers will be less than in)–32.)

umming up, therefore it appears that coronary tality as a whole in each of social classes III IV and V lower during middle age among heavy than light kers, and the hypothesis has been supported and nded This test has one considerable advantage r the first, for it provides information about categories work—heavy and light—and not merely about vidual jobs It may also be added that the excess mortality with light work is more striking in coronary rt-disease than in any of the other causes of death which the Registrar General provides data.(4)

ird Test: Physical Activity of Work and the Natural History of Coronary Heart disease

o far, these investigations have begun with *occupa al groups* involving various degrees of physical activity and have observed the rate of occurrence of cases of coronary heart-disease in them We next tried to test the hypothesis from the opposite direction by collecting *cases* of coronary heart-disease and observing their distribution among men with various degrees of physical activity in their jobs

TABLE X—MORTALITY OF HEAVY AND LIGHT WORKERS (MEN AGED 45–64 INCLUSIVE) ENGLAND AND WALES, 1930–32. SOCIAL CLASSES III, IV AND V COMBINED

Average Annual Death-rates per 1 000 000

Cause of death	Physical demands of work		
	Heavy	Intermediate and doubtful	Light
Coronary heart-disease	*264*	*359*	*456*
Myocardial diseases	*13 6*	*1 06*	*1393*
Valvular disease, &c.	*1016*	*1179*	*993*
Arterio-sclerosis without cerebral lesion	*117*	*186*	*149*
Cerebral vascular lesions	*895*	*1 03*	*1169*
Nephritis	*474*	*731*	*754*
Diabetes	*110*	*115*	*190*
Bronchitis	*683*	*851*	*522*

See footnotes to table IX and ref 13

Coronary heart-disease of middle aged men may be regarded clinically as a 'spectrum' Cases first presenting as angina pectoris belong to the benign and chronic end of the spectrum those dying in the first clinical episode of coronary thrombosis represent the other extreme of malignancy and acuteness; and between these two which may be regarded at this level of abstraction as 'minimal' and 'maximal' modes of first attack, there are various grades and stages. (The justification for such an approach lies in the unitary pathology structural and functional, of ischæmic heart-disease and in the varying prognosis in different clinical types of it.) Similarly, with deaths from coronary heart-disease deaths in *later* clinical episodes represent a more benign and chronic type of disease than do deaths in *first* clinical episodes Regarding the spectrum in terms of the present hypothesis, it may be postulated that the physical component of their work affects the chances that middle-aged men will suffer from coronary heart-disease—i.e, will get on to the spectrum (the incidence) and also how they will fare what type of disease they will suffer, and when they will die, if they do get on to it.

We may be able later to test the hypothesis in hospital outpatient departments and wards on patients with coronary *heart-disease* but this will be difficult for many technical reasons connected with the characteristic unrepresentativeness of hospital data. Meanwhile we are limiting ourselves to a preliminary consideration of *deaths* from coronary heart disease and to quite simple approaches to the natural history of the disease in terms of the mode of first presentation and the subsequent course.

HYPOTHESIS AND DEDUCTION

In heavy workers, it is postulated, the first clinical episode of coronary heart-disease is particularly likely to take the form of angina (or other relatively benign manifestation) and heavy workers are therefore less likely than light workers to die in their first episode Now coronary heart-disease is a chronic relapsing condition and men who have recovered from a *first* episode of it are liable to have later attacks in one of which they will die. If the heavier workers have a more benign form of onset and a lower case-fatality in their first episode than light workers, as the hypothesis affirms

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Analyses in these terms of heavy occupation groups and light is not particularly rewarding with other cardiovascular and related conditions Table X summarises the findings.

"There is a heavy/light trend in mortality from 'nephritis'—probably much of it hypertension[18] and a much stronger one in diabetes; but it is impossible to be as sure in these conditions as with coronary disease that the greater mortalities in the light occupations are not due in substantial part to inflation of the rates by transfer of sick men from heavier jobs. Nephritis fails on the trial of the special group of light occupations though diabetes mortality passes this trial. Many of the diabetes deaths which, because of the coding rules then in force, are best regarded as deaths in diabetic men rather than deaths from diabetes may well have been due to coronary disease and the gradient of mortality with physical activity in diabetes, may therefore be a further support of the main hypothesis (see also Joslin[3])

In the other conditions included in the table the excess mortality in the Intermediate and Doubtful column suggests that the approach is wrong that the material has been cut, so to speak, against the grain. This may be because physical activity in work is not relevant to the ætiology whatever it may be, of these conditions; or because these conditions have led to much job-changing —from heavy work to less heavy *for example* or from more skilled lighter jobs to less skilled heavier ones.

We thought of another test of the hypothesis along these lines—that the incidence of coronary heart-disease should be *inversely* correlated with conditions which are commoner in heavy workers. That this test might be useful is indicated by the Registrar General's occupational mortality data, which show an inverse relation between deaths from coronary heart-disease and deaths from accidents.[11]

they are thus more likely to have the disease in a chronic form—to suffer later episodes, and to die in a later episode It may therefore be predicted that analysis of a *representative* series of deaths from coronary heart-disease and of the occupations of the men dying (provided these have not been changed to any important extent on account of the disease) will show that

> Heavy workers have a smaller proportion of their coronary deaths in first clinical episodes of the disease, and a bigger proportion in later episodes, than light workers (Deduction A)

This deduction may be restated, that the ratio

$$\frac{\text{Deaths occurring in first clinical episodes}}{\text{Deaths occurring in later episodes}}$$

will be smaller among heavy workers than light workers It is, of course, an inference drawn from the more important part of the provisional hypothesis—that physical activity in work is associated with less severe coronary heart-disease

METHOD

We were much interested in the idea of testing the hypothesis in this way, but the only sample of death certificates available, though representative, was not really large enough for a thorough treatment of the method What follows must therefore be regarded as a trial run, a "pilot" of the proper test.

TABLE XI—NATURE OF WORK OF MEN (AGED 45–74 INCLUSIVE) DYING OF CORONARY HEART DISEASE, LONDON AND HOME COUNTIES, MARCH, 1952

Number of Deaths in Various Categories

<table>
<tr><th rowspan="3">Clinical stage of disease at which it was considered men died</th><th colspan="4">Physical demands of their work</th><th rowspan="3" colspan="2">Total</th></tr>
<tr><th colspan="2">"Heavy" work</th><th colspan="2">"Light" work</th></tr>
<tr><th>Heavy</th><th>Moderately heavy</th><th>Moderately light</th><th>Light</th></tr>
<tr><td>Row 1
Deaths in first episode
(ordinary certificates)</td><td>2</td><td>3</td><td>20</td><td>20</td><td colspan="2">45</td></tr>
<tr><td>Row 2
Deaths in first episode
(coroners' certificates)</td><td>5</td><td>3</td><td>16</td><td>14</td><td colspan="2">38</td></tr>
<tr><td rowspan="2">Row 3
Sum of rows 1 and 2</td><td colspan="2">13</td><td colspan="2">70</td><td rowspan="2">83</td><td rowspan="4">118</td></tr>
<tr><td>7</td><td>6</td><td>36</td><td>34</td></tr>
<tr><td rowspan="2">Row 4
Deaths in later episodes
(ordinary certificates)</td><td colspan="2">11</td><td colspan="2">24</td><td rowspan="2">35</td></tr>
<tr><td>5</td><td>6</td><td>13</td><td>11</td></tr>
<tr><td>Row 5
Deaths that could not be classified
(ordinary and coroners certificates)</td><td>5</td><td>8</td><td>14</td><td>11</td><td colspan="2">38</td></tr>
<tr><td>Total</td><td>17</td><td>20</td><td>63</td><td>56</td><td colspan="2">156</td></tr>
</table>

The table includes all deaths registered in the sample period in London and the Home Counties (population approx. 11½ million) except for the following

In 4 deaths the men had no occupation, or the occupation was not stated on the certificate

In 3 deaths the occupation could not be graded.

In 21 deaths the certifying practitioner did not provide further clinical information.

The true total is therefore 184

Row 5 is made up of 19 ordinary certificates and 19 coroners' certificates

Statistical significance—The distribution of deaths in row 1—where we are most certain that the episodes were "first"—is significantly different (at the 5% level) from that of row 4 but the addition of row 2 makes the difference insignificant Tests of significance based on such small numbers lose most of their value, however, in the presence of a failure rate of 36% (we are dealing mainly with 118 deaths out of a possible total of 184) On the other hand of the 66 deaths not included in the 118, there were 59 (38 from row 5 plus the 21 cases about which the practitioners did not provide further clinical information) where occupation data were available 32 of these deaths were in "heavy' workers and 37 in 'light.' It can be shown that only a very bizarre distribution of these deaths to first or later episodes (of which there is no evidence) could falsify the general support given by these data to the hypothesis.

We have copies in our unit, as said, of a representative though small sample of death certificates (kindly supplied to us by the Registrar General for another and related study[1]). The sample included all deaths from cardiovascular (and some other) conditions that were registered during the first week of March, 1952, in London and the Home Counties and a one-in three sample of those registered in the second week. The certificates for Coronary Heart Disease, coded by the General Register Office to no 420 in the Sixth Revision of the *International List of Causes of Death,*[8] were extracted In nearly all cases the certifying practitioner had provided the unit with clinical information additional to that already on the certificate It was therefore possible to classify the deaths as follows,

ORDINARY DEATH CERTIFICATES

Deaths that, judging from the information which was provided by the patients' medical attendant seemed to have occurred in the *first* clinical episode of coronary heart disease

Deaths that seemed to have occurred in *later* episodes

"Unclassifiable" deaths

CORONERS' CERTIFICATES

Coroners' certificates, after necropsy without inquest, were classified into

Deaths that occurred in hospitals (the minority)

Deaths that occurred elsewhere—mainly at home (the majority).

The latter were regarded as deaths which more probably had occurred in first clinical attacks of the disease than in later attacks, though this can only be a guess, the former, since extraneous factors enter into the decision whether deaths in hospital are notified to the coroner or no, were allotted to "Unclassifiable"

This classification was done independently by two physicians, and only cases on which they agreed were allocated to "first" or "later" categories In the great majority of certificates there was no doubt about the appropriate categorisation, where there was doubt certificates were regarded as "unclassifiable"

We thus had the following groups of deaths

(1) Deaths in first clinical episode (ordinary certificates)
(2) Deaths in first clinical episode (coroners' certificates)
(3) The sum of these—all deaths regarded as having occurred in the first clinical episode of coronary heart-disease
(4) Deaths in later episodes (ordinary certificates).
(5) Deaths that could not be classified (ordinary and coroners' certificates)

Meanwhile, we also copied the occupation from each certificate and approached two more colleagues, specialists in industrial hygiene, with the request that they grade the various jobs in terms of the physical demands of the work, and, as in the previous test, we did not tell them our hypothesis. The new occupational grading used a 4-point scale heavy physical demands—moderately heavy—moderately light—light physical demands. The experts we consulted had each independently selected this scale, they separately agreed on the allocation of nearly all the jobs, in a few, so they informed us, they agreed after discussion, in three they were unable to suggest any grading (e)

RESULTS

Table XI presents the results of this classification of deaths and jobs, the horizontal rows corresponding to the categories of deaths listed above Row 1 gives the occupational distribution of the men whose death certificates were signed in the ordinary way, and which were judged to be deaths that had occurred in the *first* clinical episode of coronary heart disease on the basis of the special information supplied by the attending practitioner 2 of the 45 men who so died were heavy workers, and 20 were light workers Row 4 makes the same analysis for men considered to have died in *later* episodes, 5 of the 35 were heavy workers and 11 were light workers Reading down the *heavy* column it can be seen that of the 17 heavy workers who died of coronary heart disease, 2 on ordinary certificates were regarded as having died in their first attack, a further 5 were coroner's cases also classified as deaths in the first episode making 7 deaths during the first attack in

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(e) Examples of the grading are

Heavy	*Moderately heavy*	*Moderately light*	*Light*
Builder's labourer Platelayer Agricultural worker	Bricklayer Sheetmetal worker Stoker	Tailor and cutter Maintenance engineer Medical practitioner	Clerk Compositor Telegraphist

XI(A)—DEATHS FROM CORONARY HEART DISEASE IN ' HEAVY ' AND ' LIGHT ' WORKERS

(Data of table XI)

NUMBER OF DEATHS

Episode of disease in which death occurred	All classes		Social class III		Social classes IV and V	
	First	Later	First	Later	First	Later
" Heavy "	13	11	1	4	11	7
" Light "	70	24	41	14	4	0

RATIOS

atios of deaths in first episodes to deaths in later episodes

	All classes		Social class III		Social classes IV and V	
	First	Later				
" Heavy "	1·2 :	1	0·25	1	1·6	1
" Light "	2·9	1	2·9	1	> 1·6	1

ers are taken from row 3—all deaths in first episode—and ow 4—deaths in later episodes—of table XI amalgamating he heavy and moderately heavy workers as " heavy " and he moderately light and light workers as " light."

ow 3 in the *heavy* column) The *light* column shows 34 of the 56 light workers were judged to have died eir first attack (20 on ordinary certificates and 14 oroners certificates) as against 11 in row 4 which considered to be deaths in later episodes. And so on able XI (A) orders the data of table XI in a form suitable testing the Deduction stated previously (f) The uction, on the whole, seems to be borne out Among " heavy " workers in all social classes combined ratio of deaths in first attacks to deaths in later cks is less than half what it is in the " light kers—13 to 11 or 1 2 1, compared with 70 to 24, or 1 If, as discussed in the Second Test, heavy kers have transferred in any numbers to light account of the disease and then died, it would mean t the number 24 is inflated and the ratio of 2 9 : 1 ong the ' light ' workers, compared with 1 2 : 1 in the eavy," underestimates the true difference in the ribution of deaths between these two groups

able XI(A) also breaks down the information by social s, and indicates why this has to be done In brief re is only one moderately heavy worker (a farmer) ong the 36 men in social classes I and II so it is not sible to test the deductions on our present data for e classes Social class III includes 5 moderately vy workers (engineering craftsmen) among the 60 s, but none of the really heavy workers Social ses IV and V, on the other hand, have all the really vy workers of table XI (they were mostly labourers various kinds) and only 4 light and moderately light rkers among the 22 deaths being considered. Since physical demands of work are thus strongly associated th social class, we had to try to make sure that under e of heaviness and lightness of work we were not merely dealing with an aspect of social class. The analysis of table XI(A) was therefore repeated *within* social class III, and *within* social classes IV and V taken together It can be seen that the deduction is also borne out within these classes so far as the numbers permit (fig 5)

The possibility that the trends of table XI are the product of social class factors is so interesting that we examined it in another way by making a similar analysis of the 67 deaths of married women from coronary heart-disease in the present sample of certificates. (The occupation given on the death certificate of a married woman is that of her husband.) The data referring to the married women showed *no* such trends as table XI(A) and Deduction A is refuted in them There was no evidence, that is to say that the *wives* of ' heavy workers in social classes III IV, and V had a different pattern of mortality from the *wives* of ' light ' workers. The nature of the physical demands of their jobs, it may therefore be proposed, affects the coronary experience of men as a direct *occupational* influence : if physical activity in work was only a reflection of *class* (or social economic) influences the natural history of the disease in their wives might well also have been affected (g)

Summing up this death certificate material which deals with current experience, thus also provides some support to the provisional hypothesis by bearing out deductions drawn from it Heavy workers there is some evidence, tend to have coronary heart-disease in a more benign and chronic form than light workers, and to die more commonly than light workers in second or later episodes of the disease. That is to say, using independent data, an association has been demonstrated or (at least there is promise of it when adequate numbers are available) between physical activity at work and the *course* of the established disease This association is complementary to that already demonstrated with incidence mode of first clinical presentation, initial severity of the disease, and early mortality rate.

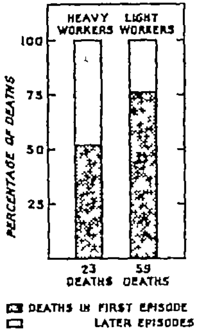

Fig. 5—Nature of work of men, aged 45–74 dying of coronary heart-disease in London and home counties in March, 1952.

III COMMENT

The present study began with observation of transport workers and the finding that one group of them the conductors whose job obviously involved considerable physical activity, had a different experience of coronary heart-disease from the drivers, whose job

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) We had not intended to extend the present study beyond 65 years of age because the other parts of it are limited to middle age. But available numbers were too small especially when it became essential to break them down by social class. The tables therefore include the deaths occurring at 45–74 years of age For the same reason it was also necessary to amalgamate the moderately heavy workers with the heavy and the moderately light with the light ; and these groups will henceforth be termed " heavy " and " light " for short. Again, to ensure sufficient numbers, the cases of row 1 could not be considered separately from the coroners cases of row 2 so that in effect rows 3 and 4 can alone be used in testing the deductions. (As the distribution of deaths at 65–74 years is very similar to that at 45–64 years, the introduction of another decade does not introduce a new element into the discussion in so far as the present problem is concerned. The other amalgamations were equally undesirable but since they made the tests more rigorous —blurring the contrast between row 1 and row 4 for instance—we thought them justifiable.)

(g) Another deduction involves a slightly different treatment of the data It may be postulated that the *duration* of the disease before death, in a representative series of deaths will be longer in heavy workers than in light workers Using only the ordinary certificates with adequate information, such an analysis shows that the deduction is borne out. Of 16 heavy workers who died of coronary heart-disease aged 45–74 years 12 died at three months or more, and 4 died in less than three months, after the clinical onset of the disease. In 59 light workers the duration before death was three months or more in 25 men, and under three months in 34

(There were 57 deaths ascribed to myocardial diseases in men aged 45–74 years in the sample of death certificates. It has been suggested that these deaths should be amalgamated with those certified to coronary disease in analysis of cardiovascular mortality ; but scrutiny of the information now available to us indicates that such a procedure would be quite unwarranted.[4 11])

obviously involved less physical activity The conductors had a lower incidence of coronary heart disease More important, the disease they had was less severe, and was less often rapidly fatal. Analysis of the experience of postal workers and Civil Servants showed a similar trend when the postmen were compared with sedentary workers.

A provisional hypothesis was then made about the relations of physical activity in work to the incidence, severity, and mortality of coronary heart disease in middle aged men This hypothesis (briefly, that physical activity in work is associated with a more favourable experience of coronary heart disease) has now been tested in three different ways—on four independent bodies of evidence, on data from the same source as the original hypothesis and on other data remote from it, basing predictions on deductions and extensions from the hypothesis as well as on parts of the hypothesis itself

None of the tests we have applied (they are all reported in part II) falsify the hypothesis, some support it strongly, some weakly The protection against coronary heart disease associated with physical activity in work has now been demonstrated, in some measure, in national, regional, and group statistics, in the mortality of three social classes separately, and of the larger occupation groups in them individually, in the morbidity from coronary heart disease of several grades of workers, as well as in their mortality, over the range of middle age and within it, when the standard of diagnosis was held constant and was probably high, and when it may have varied widely, currently and twenty years ago, before the disease was commonly diagnosed and since, on two separate gradings of physical activity, and approaching the problem through the study of "populations" as well as by the collection of cases Reliance may be placed on the cumulative effect of the regularities that have been demonstrated, however inadequate some individual pieces of evidence by themselves so obviously are Moreover, the constancy of the association in such varying circumstances encourages the hope that we are dealing with a causal relationship—the most likely origin of such a constancy The hypothesis, therefore, may be regarded as a useful one which has so far survived Several questions that arise will now be briefly discussed

PHYSICAL AND PSYCHOLOGICAL FACTORS

The most important question is about the difficulties, in this type of study, of separating observations of the physical aspects of work from observations of other aspects such as the mental and socio economic In the present instance it is quite impossible to be sure how far we have succeeded in isolating physical activity from, for example, confounding psychological factors Special pains were taken to focus on this physical dimension of work physical activity and inactivity were identified and examined in a variety of situations, and in each of them they seemed to be important variables If in fact we have been studying only, or mainly, psychological factors operating under cover of the physical, the association of these psychological factors with physical activity must be extraordinarily close, so close that no matter how the data are analysed from the physical point of view, the unknown psychological factors turn up instead or as well It is possible that psychological variables, such as work satisfaction and frustration, the presence or absence of anxiety, emotional equilibrium, or personality integration, are correlated with physical activity at work, and they may be in part produced by it But it seems unlikely that the relation between such psychological aspects and physical activity can be close and regular enough to explain in psychological terms the association with coronary heart disease that was found (a) in such a variety of occupations, and (b) in such a diversity of psychological situations The problem, it must be remembered, is not merely one of coincidence or complementarity in any particular job, but of intimate functional association of emotional equilibrium, for example, with a general physical attribute of work—its physical activity Another consideration is important There are, of course, differences in the psychological strains involved in different jobs and in the emotional support they afford, and these may apply generally to the men working in them. However, compared with such general environmental factors, the relative importance of the immediate personal situation (and what it means to the individual) is so much greater in the psychological field than in the physical that an intimate functional association of the psychological with a general physical factor, such as activity, again seems unlikely At any rate, it has yet to be demonstrated Nevertheless, it is quite conceivable that at the biological level, physical activity in work performs a stabilising function (for example in channelling so called aggressive drives) and this may be important in highly civilised societies and, for all we know, may be particularly relevant to conditions such as coronary heart disease However applicable these considerations may or may not be, it seems reasonable to postulate that physical activity of work is a relevant factor in coronary heart-disease, whether or no there also are significant psychological aspects, and whether or no these are closely associated with physical activity

POSSIBLE EFFECT OF PHYSICAL ACTIVITY ON CORONARY CIRCULATION

The next matter of interest is the possible mechanism whereby physical activity could influence coronary heart disease if the relationship is causal One relevant observation at least has been made—that men engaged in more active work do not appear merely to have a lesser total incidence of the disease but also, within this feature *more* angina This is easy to understand—that with greater effort a symptom, angina, induced by effort is commoner, and the outdoor nature of much heavy work may also be contributory Is it possible that this is all that is happening, and that everything else in the coronary circulations of the contrasting occupational groups is equal? that with more physical activity there is more angina, and that this is sufficient (by acting as an early warning signal) to produce the other and beneficial phenomenon of a substantially lower mortality

It is unlikely from the evidence (and from general experience of coronary heart disease also) that this can be the whole story If physical activity in work is effective solely by evoking the symptom of angina, certain corollaries should follow—which do not. The total incidence of the disease should be *higher* in the more active men (whatever the partition of cases between fatal and non-fatal), and it should be appearing at earlier ages because their greater exertion will be inducing symptoms and making manifest in them coronary heart

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(h) Rough and ready psychological classifications of most of the Registrar General's occupation groups of 1930-3 They were attempted by two psychologist colleagues They place little reliance on them, among other reasons because of the variety of jobs included in single occupation groups, and because of gaps in their own experience It is interesting, therefore, that in spite of these reservations some suggestive findings emerged In social classes III, IV, and V, taken together, occupation groups involving (a) "team work", (b) "little or moderate responsibility for things", and (c) "banging, bashing and cutting" (i e, expression of aggression in action upon materials or physical objects), had less mortality from coronary heart disease than their relevant contrast groups These differences are not accounted for simply by the heaviness/lightness of the occupation groups concerned disease which in sedentary workers will be quiescent and undetected. Neither in the transport workers nor in the postal workers, however is there any evidence of greater incidence among the physically more active Indeed the total incidence is somewhat lower in the conductors and postmen despite its probable inflation with the cases brought to light by greater exertion Nor is there any suggestion that the disease is appearing in the physically more active at younger ages

The proposition then that their different rate of symptom formation and manifestation (highly important influences of occupation on health), together with the consequences of these alone distinguish the physically more active group from the physically less active would appear to be an inadequate explanation of the present observations. We need, therefore to consider the possibility that physical activity acts upon the coronary circulation itself as well as influencing the demands made upon it that greater physical activity benefits the coronary circulation or lesser activity damages it or both. What mechanisms may be involved can only be guessed: whether for example there is protection (a greater ability to "cope" with thrombosis/occlusion) because of hypertrophy of arteries and small vessels with activity (an increased coronary capacity with the increased blood flow of exercise,) or contrariwise whether there is a greater liability to thrombosis or atheroma with inactivity

Satisfactory evidence is not available on the possible contribution of sunlight and outdoor life (the last of these, at least strongly associated with physically active work), or the sedentary posture (not easily separated from lightness of work) or the effects of particularly violent or sudden physical efforts which may introduce other and harmful factors[1, 9, 22] Nor are there any facts on the occupational distribution of influences that may mediate the final results—dietary habits, and obesity or hypertension for instance. Meanwhile as a first step in the investigation of possible mechanisms we hope to define the prevalence of advanced coronary atheroma in men who were engaged in different types of work, bringing together the necropsy material at the London Hospital[16] with the present hypothesis, though special studies will be needed of the architecture of the main and collateral coronary circulation and of the blood lipids.(i)

OTHER OCCUPATIONAL AND SOCIAL FACTORS

There seem to be occupational factors in coronary heart-disease other than the physical effort of the job During the present inquiries quite substantial differences in their experience of coronary heart-disease have been encountered between occupational groups where no question of a substantial difference in physical activity arises. The group of general practitioners studied, for example, appeared to have twice the incidence in 1947–50 of the other doctors.[13] (j) The nature of these other occupational factors is unknown A highly tentative attempt at psychological analysis of the occupational mortality data has already been mentioned. The other scraps of evidence which we have do not suggest that the problem is simply one of responsibility—the executive officers for instance, do not have a higher incidence or mortality than the clerks Nor does it appear that mental work as such is sufficient to transform the incidence: schoolmasters whose experience was observed in much the same way have the same rates as the intermediate group of postal workers, the postal and telegraph officers supervisors, and postmen higher grade In physical activity these four occupations are similar though scarcely in mental (The total incidence in the schoolmasters in 1949 at 35–59 years of age was 2 0—41 cases—with an early mortality of 0 8 in these postal grades taken together the figures were 2 0 and 0 9 respectively)

Osler[14] commented on the ' remarkable fact with which we are all familiar—that angina pectoris is an affection of the better classes, and not often seen except in private practice. Allbutt[1] disagreed, and of course the greater prevalence of aortic syphilis before the first world war has to be remembered in connection with such discussions The Occupational Mortality Supplement for 1930–32 recorded a considerable excess of coronary mortality in the men of social classes I and II and in the course of an interesting discussion suggested that sedentariness of work and nervous and dietary factors may be involved.[17, 19, 21] (The standard—and fashion—in diagnosis may also be important in these class differences) Differences in nutrition (so likely to be proved important in atheroma, the basis of the disease) may provide another link between the contrasting coronary experience of Western and undeveloped countries[4, 5] and between war time and normal prevalence[10]

We are thus seeking at least three sets of factors in this field

(1) Physical activity/inactivity

(2) Other occupational factors (possibly including psychological ones).

These may operate *within* the same social class as well as contributing to the differences *between* the social classes. In addition, however there may well be:

(3) Other social factors (possibly including nutritional ones)

also tending to produce differences between the social classes. There is every reason to suppose that various physical, psychological, and social factors operate together and it is quite possible that unfavourable factors cluster in certain occupational groups.

CONSTITUTIONAL FACTORS

No evidence is available from the present study on the rôle of constitutional influences, traditionally so important, and of increasing interest in chemical and physical terms[2] What we are really concerned with, in a disease that certainly has many "causes," is heredity *in* environment The bus-drivers, for instance, had been driving London buses twenty-three years on average before their first clinical attack of coronary heart-disease, the conductors had "conducted" for twenty seven (Many of the drivers had been conductors for a time before they became drivers, but there is no evidence as yet that their experience was different from that of the men who had been drivers from the start) There are many ways in which constitution and early experience may affect the incidence and natural history of disease For example, they may influence initial and later choice of job—and also be related to susceptibility to particular diseases Or, personalities of certain types, and men with certain physiques, may find what they want in light rather than heavy jobs—and develop the diseases associated with their type of personality and physique, as well as the diseases associated with light work It is premature, however, when so little is known about either constitutional or environmental factors, to attempt any assessment of the contribution of each kind of factor to the production of coronary disease The problem is similar to the psychological one in that choice of a physical *category* of work, not any particular job, would need to be highly correlated with constitutional factors which increase proneness to coronary heart disease

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(i) An incidental finding may be mentioned here. Analysing the deaths from coronary heart-disease in married women for the purpose of the Third Test it was noticed that compared with the men, they had far more of their coronary mortality in episodes of the disease later than the first. Among the men there were 83 deaths that had occurred probably in first episodes, and 35 probably in later episodes—a ratio of 2 4 : 1 In the married women using the same methods and information the numbers were 35 and 32 respectively or a ratio of 1 1 : 1 As discussed previously there is a substantial difference in this ratio between male heavy workers (1 2 : 1) and "light workers (2 9 : 1)—though not among their wives. That is to say the ratio among all married women is the same as in male "heavy workers. There are several possible explanations for this phenomenon besides the obvious one

(j) This excess, it is interesting to notice, was *over-all*, in all three main modes of first presentation of the clinical disease in angina pectoris as well as in coronary thrombosis —myocardial infarction and 'immediate mortality Such a uniform excess is unlike the pattern of the occupational differences in the disease that is the main concern of the present paper It is possible therefore that a high incidence of angina in the presence of a low total incidence, as in the conductors, (or more generally the frequency of angina pectoris as first clinical manifestation relative to that of rapidly fatal coronary thrombosis) may be an indicator that the coronary experience of different occupational groups is being affected by differences in the physical activity of these groups. When this is happening—the hypothesis might be advanced—men in the physically more active group who have a low total incidence and mortality for which their physical activity is materially responsible will nevertheless have as a discriminant feature a high absolute incidence of angina (or high, at any rate relative to the incidence of immediate ' death.) There are many possibilities in industrial medicine for testing such a hypothesis.

* * *

Since we consider that we are dealing with what is still hypothesis rather than established fact—at most an association has been established rather than a causal connection—we do not propose now to discuss the social implications of the findings It can, however, be pointed out that they may be relevant to the suggestion that there has been a real increase of coronary heart-disease in recent years—i e, during a period in which heaviness and hours of work have declined, during the second Industrial Revolution with its new sources of power, its increasing specialisation and mechanisation, in a time of growth in the scale of enterprise, with increasing numbers of men engaged in management, administration, and the bureaucracy Thus observations such as now reported may indicate future possible approaches to the prevention of coronary heart disease, though at what stages in the natural history of the disease intervention will become possible is not apparent However important the constitutional factors may be in coronary disease there is mounting evidence of variation of its incidence with environment in time, place, and society Meanwhile, we need evidence as to whether physical activity *outside* work (this may well also have diminished in recent years) in exercise and games, for example, can compensate for lack of physical activity *in* work If exercise is taken up late in a chairborne life it may conceivably even be harmful

IV SUMMARY

This report continues the epidemiological study of coronary disease and deals particularly with the relations of physical activity and inactivity in work to coronary heart disease among middle aged men

Transport workers, postal workers, and Civil Service executive officers and clerks were observed during 1949–50 Bus conductors (on double decker vehicles) were found to have less coronary heart-disease than bus drivers, and postmen less than telephonists, executive officers, and clerks Moreover, what disease the conductors and postmen had was less severe

On the basis of these observations, the hypothesis was advanced that

> Men in physically active jobs have a lower incidence of coronary heart-disease in middle age than have men in physically inactive jobs More important, the disease is not so severe in physically active workers, tending to present first in them as angina pectoris and other relatively benign forms, and to have a smaller early case-fatality and a lower early mortality-rate.

This hypothesis was tested in three ways

The early mortality-rate of conductors and postmen in 1951–52 was again found to be lower than that of the drivers and telephonists Since this "early mortality" (i e, death in the first weeks of the first clinical attack) seems to be the greater part of the *total* coronary mortality in middle aged men, an analysis was made of the Registrar General's occupational mortality data for 1930–32, this showed that at 45–64 years of age heavy workers had half the mortality from coronary heart-disease of light workers Examination of a sample of death certificates of coronary heart disease in London and the Home Counties during March, 1952, suggested that heavy workers died less often than light workers in their first clinical attack, and tended more often than light workers to have the disease in chronic form

Reference is made to possible mechanisms whereby physical activity and inactivity might affect the process of coronary heart-disease

Other possible occupational and social class factors in coronary heart disease are considered At least three possible sets of factors in this field need to be investigated (1) physical activity/inactivity, (2) other occupational factors, including possible psychological factors, (3) factors in social class, including possible nutritional factors There may be a cluster of unfavourable factors among certain occupations, particularly in the upper social classes

We are grateful to a large number of people for helping us in this inquiry the many hundreds of practitioners and hospital staff who provided us with information, the General Register Office for the certificates in the Third Test and other information, Dr R S F Schilling, Nuffield Department of Occupational Health, University of Manchester, and Dr R Murray, H.M Medical Inspector of Factories, for the classification of occupation groups used in the Second Test, Dr P H Nash and Mr R J Sherwood of the Occupational Health Sub Unit, London School of Hygiene and Tropical Medicine, for the classification of jobs used in the Third Test, the National Union of Teachers, the Teachers' Provident Society, and Mr A J Eedle, and our medical and lay colleagues in the Treasury, in other branches of the Civil Service, in the Post Office, in London Transport Executive (particularly Mr F H Spratling, Mr F J Lloyd, and Dr L G Norman), and in the Social Medicine Research Unit (particularly Dr J L E Hoffman for reading the manuscript and helping to classify the deaths in the Third Test, Dr E M Backett, who also helped to classify these deaths, and Mr V B Kanter, who did the psychological ratings of the occupation groups with him, Mrs I R Murray and the secretarial and computing staff)

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GAS-GANGRENE INFECTION IN AN OPERATING-THEATRE

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A YOUNG man sustained a closed fracture of the ankle. Next day an open operation was done, after which he developed gas-gangrene of the leg necessitating amputation. *Clostridium welchii* was isolated from the infected leg and from the floor, walls, and air of the operating-theatre suite.

Case record

On Jan. 10, 1953, a man, aged 20, fractured and dislocated his left ankle while playing football. That evening the ankle was manipulated to relieve pressure on the skin over the dorsum of the foot, and a plaster-of-paris cast padded with sterilised cotton wool was applied in the casualty theatre, which is on the ground floor.

Operation.—Next day he was operated on in theatre 1 of the main theatre suite (see figure). The skin of the ankle was incised, a large butterfly fragment of the fibula was wired, the torn joint capsule and ligaments were repaired with Mersaline sutures, and the lateral malleolus was screwed. Penicillin powder was dusted into the wound, which was closed in layers with catgut. Finally a below-knee plaster-of-paris cast padded with sterilised wool was applied. A course of prophylactic penicillin 250,000 units six-hourly was started.

Progress.—Next day, Jan. 12, the patient's temperature was 101.2°F in the morning and rose to 104.6°F in the evening. At 2.30 A.M. on Jan. 13 the operation site appeared normal. Nevertheless polyvalent anti-gas-gangrene serum 25,000 units was given intramuscularly. Later that day the patient's leucocyte-count was 23,800 per c.mm. (polymorphs 90%). A course of aureomycin 1 g. daily divided in four doses was started. On the morning of Jan. 14 pus and gas bubbles were found in the wound, and microscopy of the exudate showed many large non-sporing gram-positive bacilli and some pus cells. Culture later gave a heavy growth of *Cl. welchii* and micrococci. At midday the wound was explored under general anæsthesia. Some foul pus was present, and the peroneal muscles were pale, gelatinous, and necrotic; these were mostly excised. Portions of muscle and of catgut and mersaline sutures removed from the leg gave a heavy growth of *Cl. welchii* and micrococci. Histological examination showed a gas-producing myositis. A course of blood transfusions was started, and eight pints of blood was given during the next two days. In spite of increasing the dosage of penicillin to 1,000,000 units daily and that of aureomycin to 2 g. daily, and giving 75,000 units of polyvalent anti-gas-gangrene serum intravenously, muscle necrosis extended, and the limb was amputated above the knee on Jan. 16. Within forty-eight hours the patient's general condition improved and the pyrexia was settling. Chemotherapy was discontinued on Jan. 21, and the patient was discharged to outpatient care on Feb. 14.

Possible Sources of Infection

Since the original fracture was closed, the leg muscles are unlikely to have been contaminated by *Cl. welchii* before the operation on the ankle. However, the skin may have been contaminated with *Cl. welchii* before the operation—e.g., on the football field—and the surgical wound may have been infected from the surrounding skin. On the other hand, *Cl. welchii* may have been introduced into the wound during the operation from sources not related to the patient. Attention was focused on this possibility because the ankle was operated on in a theatre the ventilation system of which had formerly disseminated tetanus and other anaerobic spores throughout the theatre suite (Sevitt 1949).

Operating theatre

The suite (see figure) is situated on the top floor of a four-storeyed building and consists of a main corridor, two operating theatres (theatres 1 and 2), each with an anæsthetising and sterilising annexe, communicating through a central assembling room, and other rooms. The ventilation is of the exhaust type and is produced by two power-driven fans, one for each theatre. The two air outlets are situated on an outside wall, and each communicates with an independent system of air ducts and vents. Air is drawn directly from each theatre, from each sterilising and anæsthetising room, and from the assembling room into the outside air.

Strong currents of air are produced and are largely directed into the two operating theatres from the main corridor. Air is drawn into this corridor up the lift shafts and stairway. The result is that air and dust from the main corridor of the theatre and from other parts of the hospital are drawn into theatres 1 and 2 while the ventilation is on.

Moreover, since the air vents are raised about 10 ft. above the floor, upward currents of air from the floor develop within each theatre and its annexes.

Bacteriological Investigation

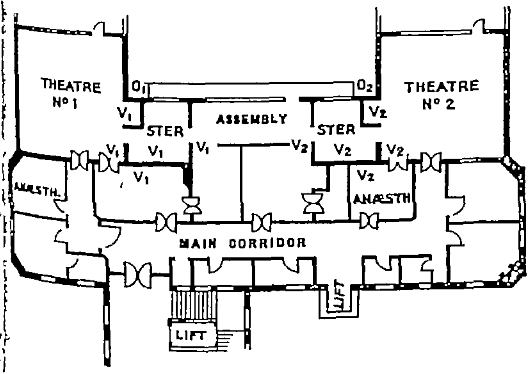
It was sought to answer the following questions:

(1) Was the dust of the floors, walls, and air of theatre 1 contaminated with *Cl. welchii*? If it was, how was this organism spread within the theatre suite, and how widely? Was the source within the theatre? This was asked because parts of the theatre walls were crumbling, and it was known that some of this wall plaster was bound by animal hair which contained various clostridia (Sevitt 1949).

(2) Were any of the operating materials used during the ankle operation, such as glove talcum powder, catgut or other suture material, plaster bandages, padding cotton wool, &c., contaminated with *Cl. welchii*?

Twenty-five swabs and portions of exposed wall plaster from different areas of the floors and walls of theatres 1 and 2, from the top of the operating lamp in theatre 1, from the walls of the assembling room and from the floor of the main corridor of the theatre suite were examined (see table).

The air of theatre 1 was sampled by Dr E. J. L. Lowbury on Feb. 28 during a surgical operation and with the ventilation working. A slit sampler was used, and narrow streams of air were sucked on to revolving discs of soft moist agar. These were broken up, and the pieces were inoculated into six flasks of cooked-meat broth.



Plan of main theatre-suite.

O_1, O_2 = fan-driven exhaust outlets of the ventilation units.
V_1, V_2 = air vents at various points in theatres and annexes.

BACTERIOLOGY OF DUST AND AIR OF MAIN THEATRE SUITE

Source and nature of specimen (no examined)		Date of collection	Bacteria present	
			Cl welchii	Other organisms
Theatre 1	Floor swabs (2)	Jan. 16, 1953	Both +	*Cl sporogenes*, A.S B, *Staph albus*, microco and coliform bacilli
	Swab from top of operating-theatre lamp (1)	,,	+	Proteus, micrococci, and A.S.B.
	Exposed wall plaster (5)	,,	2 + 3 −	A S B and micrococci
	Wall swabs (3)	March 6, 1953	−	Micrococci or A.S B. or both
	Air samples (8)	Feb 28, 1953	+	Coliform A.S B, micrococci, and other c tridia
Theatre 2	Floor swabs (2)	Jan 16, 1953	Both +	Hæmolytic strep A.S.B, and micrococci
	Exposed wall plaster (4)	,,	−	Micrococci and A.S B
	Wall swabs (4)	March 6, 1953	1 + 3 −	A.S.B or micrococci
Assembling room	Wall swabs (2)	,,	Both +	Micrococci and A.S.B
Main corridor	Floor swabs (2)	,,	Both +	Micrococci and A.S B

A S B, aerobic sporing bacilli

Seventeen specimens of plaster from the walls of theatres 1 and 2 and four from the walls of the assembling-room were removed with a sterile drill, and each was cultured in duplicate

The reels of twenty six catgut ampoules from 23 different batches (including those used at the operation), specimens from six reels of mersaline sutures, including those used at the operation, and four of 'Nylon' sutures from theatre 1 were cultured after washing to remove the immersing alcohol

Also cultured were samples of autoclaved talcum (glove) powder, penicillin powder spray, 'Benzomastic' skin paint, skin marking ink, all similar to, or identical with, those used during the operation, duplicate strips (3 × 2 in) from the inside of four plaster-of paris ('Cellona') bandages, two from the main theatre suite, and two from the casualty-theatre, and samples of autoclaved and unsterile cotton-wool both from the casualty-theatre and from the main theatre suite

Methods

The various swabs and specimens, &c, were inoculated into Robertson's cooked meat broth, when possible in duplicate, and these were incubated at 37°C The cultures were examined after 2 and 7 days' incubation and, if necessary, one and two weeks later Gram stained films were prepared, and subcultures were made on to horse blood agar plates Sometimes the broth was heated to destroy non sporers before subculturing

Identification of *Cl welchii* was based on its morphology, including the virtual absence of spores, its colonial appearance, its failure to digest the meat in cooked meat broth and the absence of other proteolytic properties except for the liquefaction of gelatin, the ability to produce acid and gas from iron peptone water media containing glucose, maltose, lactose, and saccharose and failure to ferment mannitol, the ability to precipitate a lipoprotein from human serum and the inhibition of this property by anti welchii anti toxin (the Nägler reaction), the "stormy fermentation" of milk, &c

Other bacteria were isolated and identified by the usual methods Virulence tests of clostridia were made in mice

Results

The results of the cultures from the floor, walls, and air of the theatre suite are summarised in the accompanying table

Cl welchii in the Theatre

This organism was isolated from all the swabs of the floors of theatre 1, theatre 2, and the main corridor, from the top of the operating-lamp in theatre 1, from all the cultures of the air of theatre 1, from the surfaces of the walls in the assembling-room, from some of the exposed wall plaster in theatre 1, and from the surface of one of the walls in theatre 2

Other organisms included aerobic sporing bacilli of the *Bacillus subtilis* group, various micrococci, coliform bacilli, proteus, diphtheroids, *Cl. sporogenes* and other clostridia, and a hæmolytic streptococcus.

Theatre wall plaster—Only two of the first five plaster specimens from theatre 1 and none of the four from theatre 2 yielded *Cl welchii* Since these were taken from pl crumbling on the surface and exposed to the air, the inc sistent results could have been due to irregular contaminat of the walls with air borne dust carrying *Cl welchii* spo Therefore the wall plaster was re-examined Specimens drilled out from areas where the wall paint was intact, flaming and scraping it off Four specimens each from thea 1 and 2 and the assembling room were examined, but n grew *Cl welchii* or other anaerobic bacteria, eight remai sterile It was concluded that the wall plaster was not a sou of *Cl welchii*

Cotton-wool—The unsterilised coarse brownish cotton received from the casualty and main operating thea yielded *Cl sporogenes*, a non toxigenic strain of *Cl te* another non pathogenic clostridium, and various saproph aerobes, but *Cl welchii* was not found. This kind of cott wool is commonly used to pad plaster of paris casts over clo fractures Interesting as these findings are, they are proba irrelevant to the present investigation, because the cott wool used under the plaster casts of the present patient autoclaved white cotton-wool

Plaster-of paris bandages grew only an aerobic long slen gram positive bacillus, probably a sporer

The various specimens of *catgut*, *mersaline* and *nylon sutu* *talc powder*, *penicillin powder*, *benzomastic paint*, and *marking ink* were sterile except for cocci or diphther contaminating the mersaline and nylon reels

Efficiency of theatre autoclaves—Tests had last been d four weeks before the operation and were then satisfacto Tests made a few days after the operation showed that au claving at 20 lb for 20 minutes (dressings) and at 15 lb. 15 minutes (gloves) killed the test *B subtilis* spores

Discussion

The investigation of the source and route of infecti with bacteria like *Cl welchii*, which cannot yet divided into different phage or serological types, is fraug with difficulty Direct proof is virtually impossible wh the event is over, and a judgment can only be based indirect and circumstantial evidence Such was the sit in the present investigation

Since *Cl welchii* was isolated from the gas gangren muscle of the patient it is considered to be the bacte cause of the infection *Cl welchii* was also present only in the air and dust of theatre 1, where the an was operated on, but also was widely distributed in dust throughout the main theatre suite Specimens talc powder, suture material, &c, similar to, or identi with, those introduced into or near the patient's wou did not contain *Cl welchii*

It is therefore reasonable to conclude that the air theatre 1 contained welchii spores during the operat on Jan 11, and that aerial contamination of the patien ankle took place then

Similar contamination of surgical wounds at oth times must have happened Nevertheless, postoperat gas gangrene is very uncommon This is because co tamination is not infection For gas gangrene to devel more than the right bacteria are required, mus ischæmia or necrosis or sepsis or other factors are nec ry In the present patient ischæmia of the peroneal muscles due to arterial spasm may have been present nd have provided the necessary tissue conditions for the *evelopment of gas gangrene.*

xhaust Ventilation

The real villain of the piece is the exhaust type of entilation which sucks air and dust from the hospital nd theatre corridors and from other parts of the hospital nto the operating theatres In other words, each theatre ecomes an "air sewer" draining much of the hospital ir and dust and, since dust commonly bears spores of l. *welchii*, the theatre suite is widely contaminated with his organism. Other ways of spreading *Cl welchii* may ave occurred, such as the contamination of the theatre orridor floor by dirt from the soles of shoes.

Further, upward draughts towards the vents suck loor dust into the air Every wound made or exposed in he theatre is therefore exposed to floor-dust bacteria ncluding *Cl. welchii*. Moreover wounds have been nfected with other bacteria, such as the two cases of etanus which were traced to aerial dissemination of etanus spores by the same ventilation plant (Sevitt 1949).

Air Hygiene for Operating theatres

Exhaust ventilation was originally introduced into operating theatres to remove steam from the sterilisers and to make the theatre comfortable for the surgeon and the theatre staff to work in Though this is a highly admirable purpose, the problem of designing ventilation to minimise wound infection as well as to ventilate the theatre was not considered until recently Bourdillon and Colebrook (1946) introduced an air-conditioned room for the dressing of burns. Filtered warmed, and humidified air is passed into this dressing room from the ceiling by a forced ventilation plant and is extracted at floor level. This ensures "an atmosphere almost free from bacteria at the start of the dressing and a rapid evacuation of organisms disseminated through the air in the course of each dressing"

The incidence of added infection due to hæmolytic streptococci, *Pseudomonas pyocyanea*, and proteus among the burnt patients was greatly reduced after the introduction of this dressing station (Colebrook et al 1947, 1948). A controlled trial now in progress has already confirmed the reduction of added infection with *Ps pyocyanea* and other coliform bacilli when the burns are dressed in cleansed air (E J L Lowbury, personal communication)

If ventilation systems designed to control the hygiene of the air within operating theatres were introduced it is highly probable that the incidence of surgical wound infection would decline. In particular, aerial dissemination of tetanus and *Cl. welchii* spores, such as gave rise to the previous and present investigations, would not occur

Surgeons and hospital authorities who insist on sterile gloves and instruments for operations should be equally particular about the cleanliness of the air in their theatres. Clean air is desirable in all theatres but is of high priority in those dealing with traumatic, thoracic orthopædic and neurosurgical cases, in all of which the hazards or results of infection are particularly serious.

Summary

An open operation was done on a closed fracture of the ankle. Gas gangrene followed, and the leg had to be amputated: *Cl. welchii* was isolated from the infected muscle.

An investigation showed that the floor, walls, and air of the operating theatre were contaminated with this organism It was known that the exhaust ventilation of the theatre suite sucked air and dust from much of the hospital into the operating theatre and disseminated this dust within the theatre. It was therefore concluded that aerial contamination of the wound took place during the operation and that this was brought about by the air currents produced by the ventilation

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CORTISONE AND RHEUMATOID DISEASE

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Many papers have been written during the last four years on the use of cortisone in the treatment of rheumatoid disease The profound effect of this hormone especially in a daily dosage of 100 mg or more, on the symptoms and signs of the disease in the early weeks of treatment is acknowledged by all Unfortunately doses bigger than 75 mg a day can rarely be maintained for many months without serious complications. It has yet to be shown whether a restricted dosage of 50–75 mg a day is worth while Many favourable opinions have been expressed but they have not been backed by the kind of evidence that one expects from the clinical trial of a new treatment (see Tenth Rheumatism Review 1953)

The present study was made to provide a definite answer to the question whether the oral administration of cortisone acetate 50–75 mg a day continued for a long time, favourably affects the course of rheumatoid disease or not

The Treated Group

31 patients with rheumatoid disease were started on long term cortisone treatment from one to three years ago 1 fell out after three months, 3 died after a year's treatment, and the remaining 27 (table I) are still receiving cortisone to date The progress of the 27 patients will be considered first. The average duration of daily cortisone *acetate therapy for this group is nineteen months.*

At the beginning of treatment each patient had many joints affected (clinically and radiologically), the disease was active, and the erythrocyte-sedimentation rate (E.S.R.) was above 15 mm in 1 hr (Wintrobe) According to the classification of Steinbrocker et al. (1949) 16 patients were in stage II and 11 in stage III.

TREATMENT

In the early months of the investigation cortisone acetate was given by intramuscular injection For the last two and a half years it has been given solely by mouth The dose given during the last two years has fluctuated between 50 and 75 mg a day, occasionally

TABLE I—DESCRIPTION OF PATIENTS

—	No	Age range (yr)	Average age (yr)	Range of duration of disease (yr)	Average duration (yr)
Men	12	35–60	46	2–33	7
Women	15	18–51	41	1½–16	5½

exceeding 75 mg for a week or two when the symptoms and signs have been most acute In addition each patient has been given physiotherapy, mainly active Only 1 patient has been able to dispense with aspirin or compound codeine tablets for more than a few months The average patient has needed at least eight tablets a day for most of the time It would not have been possible to stop these patients from resorting to aspirin

RESULTS

To assess progress the patients have been seen at least every four weeks for interrogation, for physical examination of joints, grip, weight, blood-pressure, &c , and for laboratory investigations—E S R , hæmoglobin packed-cell volume, eosinophil-count, and plasma protein, plasma fibrinogen, and plasma cholesterol levels

A sound idea of the results of treatment in rheumatoid disease may be gained by answering the six questions below In assessing the results for any treatment for rheumatoid disease it is essential to make as much allowance as possible for the natural fluctuations in the activity of the disease It is so natural to select patients for a new treatment at the height of an exacerbation and to be misled into believing that the improvement, which would have come about naturally in many cases, has been due to the treatment Consequently the clinical assessments given below are those for the six months before treatment began and for the last three months of treatment The laboratory data represent the average of readings during the same periods

(1) *Have the affected joints ceased to stiffen with rest?*

96% of the patients still have joints that stiffen with rest The intensity of the stiffness in an affected joint and its duration after a night's rest provide in most cases of rheumatoid disease the simplest means of assessing the activity of the disease

(2) *Are analgesics still necessary to relieve pain and stiffness?*

89% still find analgesics necessary to obtain relief from pain and stiffness Aspirin is the best friend of the rheumatoid patient When a patient says that she cannot manage without aspirin, this is almost invariably a true symptom of continuing activity of the disease

(3) *Can the patients do more?*

As a group they have been able to do more in recent months than in the six months before treatment, but the increase is small The meanings of the numbers P1–P5 in the tables are as follows

P1 able to work and play as a normal person of the same age

P2 able to do light work without real difficulty but unable to manage heavy work or vigorous games because of the rheumatoid disease

P3 able to do light work only with considerable difficulty , taking some hours to limber up each day , poor grip and considerable limitation in walking and on stairs

P4 only able to struggle round indoors with aids , needing help to dress and to get up and down

P5 bed fast , unable to stand or to attend to simple needs

Patients often fluctuate between grades P2 and P3 in a few months When this has been the case during a period of assessment (table II), they have been graded as P$2^1/_2$ In no case has the reduced physical ability been due mainly to burnt out rheumatoid arthritis

(4) *Has the E S R fallen?*

The average E S R before treatment was 34 mm in 1 hr (Wintrobe) The average E S R during the last three months of treatment was 29 mm in 1 hr (Wintrob Only 2 patients have had an average E S R. below 15 m in 1 hr during the last three months

TABLE II—ASSESSMENT OF RESULTS

Physical ability (P grades)	Improved by			No change, at		Worse by
	2	1	$^1/_2$	P3	P$2^1/_2$	$^1/_2$
No of patients	1	5	8	6	5	2

(5) *Has the anæmia, the raised plasma fibrinogen level, a abnormal albumin-globulin ratio associated w rheumatoid disease been corrected?*

The average Hb before treatment was 11 3 g per 1 ml , and in the last three months of treatment 12 3 per 100 ml The average plasma-fibrinogen level bef treatment was 0 42 g per 100 ml , and in the last th months of treatment 0 34 g per 100 ml The aver albumin-globulin ratio was 1 6 1 both before treatme and in the last three months of treatment

(6) *Do radiographs of affected joints taken at the beginn of treatment and recently show evidence of at least arrest in the disease?*

There was new or increased bone erosion in 16 (60% no change or absence of bone erosion in 8 (30%) , hea bone erosion in 1 , and doubtful erosion or not kno in 2 It was impossible to make a scientific assessmen changes in bone density Our opinion is that in onl cases had bone density definitely improved In 1 of th patients fresh erosions had developed in other bon Where there was reasonable doubt about the appeara of new erosions or the extension of pre existing erosio the result was recorded as " no change "

According to Steinbrocker's criteria of improvement patient is in complete remission, 4 patients show mark improvement, 4 show minor improvement, and 19 unchanged

Controls

The impression gained from many published studies differing methods of treating rheumatoid arthritis that at least 15% of patients recover and at least 5 are much improved The results given above appea to fall so far short of this standard that it was conside very necessary to assess by the same criteria a sim group of patients who had not received cortisone

From about 1000 cases seen in recent years 27 w selected to pair with individual cases in the cortiso treated group The patients naturally had to be of same sex and under our observation during the sa time They were selected as most nearly resembling th cortisone treated opposite numbers as regards age, du tion of disease, and distribution of affected joints for instance, a given cortisone-treated patient, aged had had the disease for four and a half years, and h the joints of all four limbs involved, then a control w selected who most closely resembled him in th particulars

Comparisons

(1) *Joints stiffening with rest*

Cortisone group 96%
Paired group 89%

(2) *Need for analgesics*

Cortisone group 89%
Paired group 93%

(3) *Physical ability*

Cortisone group before, P3 , recent, P2 7
Paired group before, P2 6 , recent, P2 3

(4) *E S R (Wintrobe)*

Cortisone group before, 34 mm. , recent, 29 mm
Paired group before, 23 mm , recent, 25 mm.

(5) *Hæmoglobin*

Cortisone group before, 11 3 g , recent, 12 3 g
Paired group before, 13 5 g , recent, 13 2 g (M.R method

The hæmoglobin estimations for the cortisone treat patients were made by an oxyhæmoglobin method w a standard checked by gas analysis experiments. T M R C method is generally known to give high readi —about 8% above those given by the other method is concluded that the hæmoglobin values today in bo groups are about the same, and that in neither group have they risen to average normal levels Plasma protein and plasma fibrinogen levels were not estimated as a routine in the paired patients

(6) *X ray changes*

Of the 27 controls only 20 had suitable films taken at the appropriate times. Of 20 pairs there was an advance in erosions in 15 of the cortisone group and 12 of the controls.

(7) *Strength of grip*

One expects men to be able to send the mercury up to the top of the sphygmomanometer scale (260 mm.) and women to at least 200 mm The results were as follows

Cortisone group : latest reading right 135 mm. left 153 mm.
Paired group latest reading, right 122 mm. left 116 mm.

The interpretation of this difference is complicated by the fact that the paired group had their readings taken in the morning, whereas most of the cortisone treated group had their reading taken in the afternoon The physical abilities of most patients with active rheumatoid disease improve as the day wears on and are usually maximal by mid-afternoon

Well-being

Much has been said of the increased well being that cortisone treatment imparts to rheumatoid patients. This is undoubtedly the case in the early weeks of treatment, but it falls off in time. Whether any remains after a year's treatment is difficult to assess. No attempt has been made to assess and compare the sense of well-being in the paired group

DISCUSSION

The evidence so far presented shows that the administration of cortisone acetate, as described above does not have a favourable effect on the course of rheumatoid disease. It may well be asked why it is that in spite of continuing disease activity in both groups the average physical ability of the patients improved. The answer is that in a unit devoted almost entirely to the investigation and treatment of rheumatoid disease vigorous measures are taken to restore muscle power so far as is possible, and to retain it also to prevent and to correct deformities. But for these measures some patients would have sunk to category P4.

Complications

Infections mental and endocrine disorders operations—No abnormalities as regards infections and inflammations, mental behaviour or the endocrine system have been noted during a prolonged treatment with oral cortisone acetate in the restricted dosage The X ray appearances of the lungs have remained unaltered. Three major and some minor operations have been done without untoward happening For these operations the dose remained unaltered—it might have been wiser to raise it temporarily (see theoretical discussion below)

Gastric hæmorrhage—There have been five instances in 3 patients. No hæmorrhage occurred in the controls The bleeding occurred in spite of precautionary advice on diet and the use of antacids.

Osteoporosis—No evidence of a general increase in bone porosis has been noted but 1 patient a man aged [illegible] with long-standing disease, had a pathological fracture of the neck of the femur An acrylic prosthesis has remained satisfactory to date (eight months) Only 1 patient had open epiphyses they closed normally

Weight increase—The average weight before treatment was 59 kg. and in the last three months of treatment [illegible] kg. Of the paired patients only 22 had weight records at about the same intervals Of the 22 pairs the average weight of the cortisone-treated patients before treatment was 60 kg. and in the last 3 months of treatment 66 kg whereas of the controls it was 61 4 kg before treatment and 6[illegible] 7 kg in the last three months of treatment. The difference in increase is 4 7 kg (10 lb) This increase in weight has not bothered the men but some of the women do not appreciate what they consider to be a disproportionate increase about the hips Many have faces fuller than normal. The weight increase is mentioned under complications since it is of abnormal distribution and not related to a subsidence of disease activity

Enlargement of heart—When the chest films were being examined for evidence of tuberculosis, it was noted that in many cases the heart appeared to have increased in size On close examination it was found that of the most recent films 17 showed a raised diaphragm, 4 a lowered diaphragm and 6 no change The films were referred to Dr T Lodge for an opinion about alteration in heart size He gave his opinion that 6 showed definite enlargement These 6 comprised the 4 with the lower diaphragm, 1 with an unaltered diaphragm level and only 1 of the 17 with a raised diaphragm level. One wonders how many more would have been considered enlarged had there been no raised diaphragm to complicate the assessment It seems most likely that increase in fat in the omentum and in the abdominal wall accounted for the elevation of the diaphragm

Blood pressure—The average blood pressure before treatment was 131/79 mm Hg and the average of the last two readings 135/84 mm Hg Unfortunately too few of the paired patients had blood pressure readings at the appropriate times to allow a comparison One can at least infer that for the group as a whole there was no gross increase in blood pressure

Serum-cholesterol level—The average total serum cholesterol level before treatment was 143 mg. per 100 ml, and in the last three months of treatment 160 mg per 100 ml. In only 1 patient did the total serum-cholesterol level exceed 200 mg per 100 ml.

Leucocytosis—At the start of cortisone treatment there is usually a considerable leucocytosis In this study the average rise was from 7700 to 11 400 per c mm The average of the last (most recent) two readings for the group was 9200 per c mm The average counts for the paired group were 8100 per c mm at the beginning and 7300 per c mm at the end In considering whether the treatment given has been physiological or not this rise in the total white-cell count must be considered. The lymphocyte-count appeared to remain stable More than eight hundred eosinophil-counts were made during the study In only 1 patient did the counts remain below 50 per c mm. ; in 6 they remained less than 100 per c mm., and in 9 they exceeded 200 per c mm

Withdrawal syndromes—Relative adrenocortical deficiency and acute deficiency at times of stress may follow the withdrawal of cortisone acetate after prolonged therapy Such states were not observed in this study but must be considered when evidence for and against this therapy is weighed. Now that a comparatively simple laboratory assay of the adrenals output of hydrocortisone is available (Norymberski et al 1953 Brooks and Norymberski 1953 West 1953) it is not difficult to find out whether the adrenal function has been restored, and whether a normal response follows the administration of corticotrophin This still does not tell us whether the pituitary has been restored to normal activity and whether it can respond to severe stress Little is known of the stresses in man that call for a rapid increase in adrenocortical activity, but it is known that the stress of a major operation may call for the secretion of 100 mg or more of hydrocortisone in twenty four hours

Fatalities

The first 2 deaths have been fully reported (West and Newns 1952) Both patients had received cortisone daily for about a year One died of amyloid disease, and the other died suddenly after having been without cortisone for four days In neither case could death be ascribed to cortisone therapy, but in both cases death was undoubtedly hastened by its use

The third patient, a man aged 36, developed polyarteritis nodosa He was a typical case of rheumatoid disease, the signs having appeared first in the proximal interphalangeal joints two years before cortisone therapy was begun The first symptoms suggesting polyarteritis appeared in the fourth month of treatment The dose of cortisone was increased, but he died five months later as a result of hæmorrhage from one of many gross intestinal arterial lesions Lesions developed with a prolific cellular exudate while he was receiving cortisone acetate 150 mg a day This single case might not be considered remarkable but for the occurrence of similar cases in the U S.A Levin et al (1953) reported 3 such cases in their series, and we have heard indirectly of several others in the U S A. The cortisone treatment must be held at least partly responsible until more evidence is available

Theoretical Considerations

Is there any theoretical reason why cortisone should have a curative effect in rheumatoid disease ? There is not No abnormality in corticosteroid metabolism has been confirmed in this disease This does not exclude the existence of an abnormality, since comparatively little is yet known of the metabolism of corticosteroids or of the essential rôle they play in the tissues, or of the tissues' needs We have now estimated the total urinary output of the known metabolites of cortisone and hydrocortisone (as 17 ketogenic corticosteroids) of 30 rheumatoid patients, and have found their output on the average about 40% below that of normal controls When these levels are raised to those of normals, however, the disease does not appear to be significantly affected The levels can be raised by the administration of either corticotrophin or cortisone acetate

Are there theoretical reasons for condemning the administration of cortisone acetate (in the doses used above) for a long time ? It may be held that a hormone is being administered in unphysiological amounts, regardless of the diurnal variation of the body's needs and regardless of the need for considerable variations during certain stressful episodes The doses given correspond to less than the natural output during the stress of a major operation, but they correspond to twice the normal day-to day secretion Evidence of the unphysiological nature of these doses may be seen in the patient's increase in weight and possibly in the raised total white-cell count

Some evidence has been provided in our laboratories that cortisone acetate 50 mg administered daily will completely suppress the endogenous output of hydrocortisone-like steroids (Norymberski et al 1953) Does this matter ? So far we have no evidence that it does What does matter is the consequence of stopping cortisone therapy after the adrenal production of hydrocortisone has been suppressed for a long time

Conclusions

Cortisone acetate given for a long time in doses of 50–75 mg a day does not favourably influence the course of rheumatoid disease It does not necessarily follow that prolonged administration is not of benefit in certain types of rheumatoid disease Claims for such benefit have not yet been substantiated by controlled studies

In attempting to justify the prolonged use of cortisone acetate, the early benefit enjoyed by some patients and the possibility of some continuing improvement in well-being must be weighed against complications that cannot necessarily be foreseen or prevented Until such complications can be avoided with certainty the long-term stration of cortisone acetate for rheumatoid cannot be recommended

Does this mark the end of a chapter ? We do not think so for two reasons

(1) A dose of 50 mg of cortisone acetate produces a profound effect in some cases of rheumatoid disease, particularly in some long standing cases Now such a dose has not been shown to relieve any other kind of inflammation. The fact that these good effects are not maintained suggests that some adaptation takes place to the raised level of circulating corticosteroid Preliminary studies have not shown any alteration in the total excretion of cortisone metabolites following prolonged therapy (unpublished data), but the possibility remains that an alteration in the metabolism of cortisone does take place which, when understood, may help us to overcome the loss of therapeutic effect

(2) Far too little is known of the metabolism of corticosteroids to exclude them from an important rôle in rheumatoid disease or in hypertensive diseases or in some forms of cancer.

Summary

Cortisone acetate 50–75 mg daily has been administered to 27 patients with rheumatoid arthritis for an average of nineteen months A further 3 patients treated in this way died after nine to thirteen months

A comparison has been made with a similar group of 27 patients who did not receive cortisone

The conclusion has been reached that long-continued cortisone therapy for rheumatoid disease is not to be recommended

The observations recorded are not thought to exclude corticosteroids from a rôle in the pathogenesis of rheumatoid disease

Most of the cortisone acetate used in this study was provided by the Medical Research Council and Nuffield Foundation joint committee on cortisone and A C T H in chronic rheumatic diseases, to whom our thanks are due Particular thanks are due also to both the patients and the nurses for their loyal coöperation

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A SKIN TEST FOR MUMPS
USING CEREBROSPINAL FLUID FROM CASES OF MUMPS MENINGITIS

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During the last epidemic of mumps in Athens we often observed cases with involvement of the central nervous system 107 patients presenting symptoms of meningitis were treated in our clinic

Montenovesi (1952), reporting an outbreak of epidemic parotitis in Verona in 1951, mentions 54 cases of meningitis He cites Fox and Grotts (1949), who described 23 cases of meningitis among 35,322 patients with mumps, of Hack (1910), who found 9 cases among 476 patients, of Gott (1950), who found 10 cases among 3306 patients, and of Cozza and Capretti (1948), who found 27 among 55 patients

The meningo encephalitic symptoms, which appear occasionally before or without involvement of the parotid glands, are not only of practical diagnostic importance but be of theoretical interest. It is now well established hat the meningo-encephalitic symptoms are due to nfiltration of the virus into the central nervous system

The virus has been isolated from the cerebrospinal fluid c.s.f) of patients with mumps and cultured (Levaditi and Lépine 1948, Klöne 1952) Fanconi et al (1945) distinguish wo types of involvement of the central nervous system—1) meningitis due to the direct damage of the cells by the rus (early type) and (2) encephalitis due to serous non pecific inflammation of the Rössle Eppinger type as a result f antigen-antibody reaction (late type)

It is well known that mumps leaves immunity which s transmissible and can be studied by complement xation, hæmo-agglutination inhibition tests and skin ests. The development of the skin tests is largely due to he work of Enders (1943) By injecting a suspension f parotid gland, obtained from an infected monkey and nactivated at 65°C for twenty minutes, intradermally nto patients who had had mumps he obtained an rythema and infiltration of 1–4 mm in diameter at the ite of injection in almost 100% The reaction lasted two o four days. The injection of parotid gland suspensions from non infected monkeys produced no reaction

According to Enders the skin test is usually positive when done at least a week after the onset of mumps The dermal hypersensitivity may last up to two years after the onset of mumps. On the other hand the reaction is found positive in 50% of people with no history of mumps The same holds for the complement-fixation test.

The practical importance of the skin test is diminished by the fact that monkey parotid glands are not easily obtained. Habel (1945) has got better results with a suspension of egg yolk from infected chick embryos

We report here a simpler method of proving skin hypersensitivity to the mumps antigen It is based on the fact that the virus of mumps is present in the c.s.f of patients with mumps meningo-encephalitis

Investigations and Findings

We used c.s.f of such patients The involvement of the central nervous system was confirmed in these cases by examination of the c.s.f Increased pressure and a slight increase in the amount of albumin were often found, but an increased white-cell count (mainly lymphocytes) was the constant finding At times it was so high that it gave a cloudy appearance to the c.s.f

The samples of c.s.f were initially obtained on the fifth, tenth, and fifteenth days of the illness. They were inactivated at 65°C for twenty minutes and centrifuged at 2000 r.p.m for thirty minutes. The sediment was diluted and injected intradermally

We first tested 72 patients with mumps or with a history of mumps, and 28 without such a history The results differed according to the day of the disease on which the specimen of c.s.f was taken :

C.S.F *obtained on the fifteenth day* was injected into 21 patients with mumps. There was no reaction.

C.S.F *obtained on the tenth day* was injected into 17 patients with mumps No reaction was noted

C.S.F *obtained on the fifth day* was injected into 34 patients with mumps or recovering from mumps and into 28 controls with no history of mumps. As the accompanying table shows, the reaction was positive in all except the controls, the red area measuring 3–10 mm and the zone of infiltration 2–6 mm. In a few cases redness and infiltration reached 2 cm., and in 1 case we observed a blister as big as a pea. The reaction obtained by this method is much more intense than those described for the older methods.

In 150 children at an orphan asylum where there was an outbreak of epidemic parotitis recently, the reaction (with c.s.f taken on the third day of the illness) was positive in 30 (90%) of those who had had mumps in the previous six months, in 19 (74%) of those who had had mumps between six and twelve months previously, and in 26 (65%) of those who had had it one or two years previously The reaction was also positive in 75 (10%) of the children with no history of mumps, but, since the children are orphans an accurate past history was difficult to obtain Even if they had really not had mumps, a positive skin test might be explained on the basis of immunisation by contact with the virus. Enders et al (1945) *obtained positive reactions in 50% of people with* no history of mumps.

By further tests carried out with c.s.f taken during the first five days of the illness we have found that this sample has considerable antigenic properties which are present on the first day of the illness, are greatest on the third day and decrease gradually until they disappear on the tenth day The strongest reaction is obtained during the two or three months after the subsidence of the attack of mumps, but skin hypersensitivity is still present after six months. How long it continues we do not yet know

We have obtained positive reactions with a dilution of 1 in 10 000 The usual dilution which gave us 100% positive reactions was 1 in 10 (see table) (It may be mentioned that the supernatant c.s.f after centrifugation also gave positive but less intense reactions) We are studying how long the c.s.f can keep its antigenic properties We have reasons to believe that when it is kept at 4°C it can remain active for a time.

The specificity of the reaction has been controlled with cross skin reactions. c.s.f from poliomyelitis, infectious mononucleosis lymphocytic choriomeningitis, and chickenpox was injected intradermally into patients with mumps and c.s.f from patients with mumps meningitis was injected into patients with those diseases. No positive reaction was obtained.

Summary

In mumps meningitis the c.s.f has strong antigenic properties Its antigenic potency reaches its peak about the third day of the illness and decreases gradually until it disappears by the tenth day

RESULTS OF SKIN TESTS WITH C.S.F TAKEN ON FIFTH DAY OF ILLNESS

C.S.F sample no.	Case no.	Day of illness	Dilution of C.S.F		
			1 : 10	1 : 100	1 : 1000
	Patients with mumps				
1	1	8	++	+	+
	2	9	++	+	+
	3	15	++	+	+
	4	11	++	+	+
	5	10	++	+	+
	6	5	++	+	+
	7	3	++	+	+
2	8	17	++	+	+
	9	13	++	+	+
	10	8	++	+	+
	11	7	++	+	+
	12	9	++	+	+
	13	6	++	+	−
	14	5	++	+	+
	15	6	++	+	+
	16	4	++	+	+
	17	9	++	+	+
3	18	4	+	+	−
	19	6	++	+	+
	20	5	++	+	+
4	21	7	++	+	+
	22	9	++	+	+
	23	7	++	+	+
	24	8	++	+	−
	25	7	++	+	+
	26	9	+	+	+
	27	5	+	+	+
	28	4	+	+	+
	29	5	+	+	+
	30	6	+	+	+
	Patients with history of mumps				
2	31		+	−	−
	32		+	−	−
	33		+	−	−
4	34		+	+	−

Specimens of C S F kept at a low temperature can probably maintain their antigenic power for some time

Using C S F obtained from patients with mumps meningitis on the fifth day of their illness, in a dilution of 1 in 10, a positive skin reaction was seen in all the persons tested who were suffering from mumps or had a recent history of mumps The reaction was positive as long as two years after the infection

Reactions were also positive in about 10% of children who were not known to have had mumps No reaction was obtained in cases of poliomyelitis, infectious mononucleosis, lymphocytic choriomeningitis, or chickenpox

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HEPATIC VENOUS HUM IN CIRRHOSIS OF LIVER

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Venous hum in cirrhosis of the liver was first reported by Pegot (1833), whose patient, an alcoholic ex soldier, presented with a caput medusæ whose centre at the umbilicus was a widely dilated vein as large as an orange The hum was audible over a restricted area of this dilatation in the immediate vicinity of the umbilicus The necropsy findings were described by Cruveilhier (1835) Since then other reports have been published, and Bloom (1950) collected 60 published cases and reported 2 further ones

Catti (1907) and, independently, Thayer (1911) first emphasised the superficial origin of the hum They considered that it was produced in collateral veins in the abdominal wall by the rapid passage of blood through a relative constriction into a dilated segment All subsequent accounts, with two exceptions, have subscribed to this view Huber et al (vide Florand 1922) thought that the first hum which had developed in the case reported by Florand (1922) was due to an arteriovenous shunt, and Bates (1937) considered that the hum in his case resulted from constriction of the inferior vena cava by perivenous hepatic fibrosis—a view first advanced by Gambarati (1903)

While in most cases the collaterals are subcutaneous and visible, in many none are seen In these latter necropsy has revealed collateral channels in or deep to the rectus muscles, and the most frequently encountered localised dilatation lies immediately superficial to the xiphoid process, the area in which the hum is most commonly heard Lutembacher (1936) reported a case in which a venous hum could be heard in two sharply defined areas over the xiphoid process, where no collaterals were visible, and some 2 cm away from a saccular dilatation on a subcutaneous varicose vein At necropsy a large dilated vein was found on the deep aspect of the rectus muscle, and immediately under the areas in which the hum had been heard there were [illegible] dilatations

Those reported cases of venous hum which have established beyond dispute as being produced in colla channels have certain characteristics The hu localised to an area of at most a few centimetr diameter and is not propagated along the vein in whi arises Although varying in intensity it is loud or roaring, continuous, and in most cases increased by inspiration In most cases there is a palpable thrill the site of the hum, and this is invariably present the hum arises in a subcutaneous collateral

We report here a case of cirrhosis of the liver in w a venous hum was heard which differed in many res from that described above and probably had its o in arteriovenous shunts in the liver

Case-record

A Chinese carpenter, aged 32, was admitted to the Ui sity Department of Medicine, Queen Mary Hospit November, 1952 His only complaint was of an abdo mass to which his attention had been drawn by disco while wearing a tight belt some four months before admi

He had been born, and had resided all his life, in Hong Kong and, save for irregular attacks of fever between 1937 and 1945, one of which was established as being due to malaria, his previous health had been good

On examination he was healthy looking, well developed, and muscular The abdominal mass was found to be an enlarged mobile non tender spleen, the lower pole being defined 6 cm below the costal margin in the mid clavicular line The liver was not felt were no visible collateral veins The presence of a amount of free fluid was demonstrated in the abd The only other abnormality detected on physical e nation was a murmur heard over a wide area exte from the right mid axillary line over the lower thoracic cage anteriorly into the upper epigastrium upwards in a narrow area on both sides of the sternu the fourth intercostal space Over the right thora murmur was distant, it became suddenly louder i immediate vicinity of the xiphoid process and when upwards on either side of the sternum it rapidly dimin disappearing above the fourth intercostal space The dis tion and relative intensity of the murmur are depict fig 1 It was a continuous humming sound which in all had a distinct systolic accentuation almost synchronou the radial pulse It was not influenced by the pha respiration, nor was it affected by changes in posture thrill could be detected on palpation

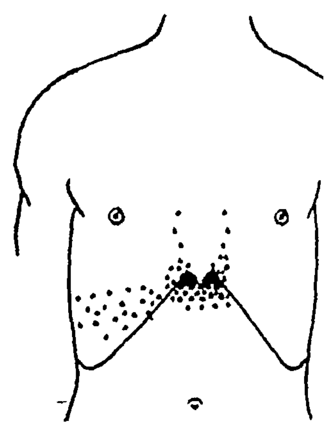

Fig 1—Distribution and intensity of v hum

Investigations—A barium swallow demonstrated presence of œsophageal varices, and the appearanc aspiration liver biopsy were those of a diffuse hepatic fi A blood count showed hæmoglobin 9 2 g per 100 ml., re 3,200,000 per c.mm, mean corpuscular volume 90 c.μ, cells 2200 per c.mm (neutrophils 39%, eosinophils lymphocytes 59%), and platelets 84,000 per c.mm S marrow biopsy showed normoblastic erythropoiesis hyperplasia of both erythroid and myeloid series a increased number of megakaryocytes

Diagnosis—Diffuse hepatic fibrosis and gross splenom with pancytopenic hypersplenism were diagnosed.

Operation—Splenectomy was considered the only trea because there was no history of gastro intestinal hæmor and the amount of the fluid in the abdomen was sma readily controlled. The abdomen was opened through a line incision The liver was smaller than normal and sl diffuse hepatic fibrosis. Running in the falciform ligam

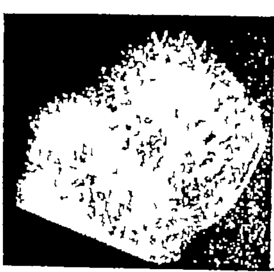

Fig 2—Hepatic arteriogram (left lobe) in reported case of cirrhosis, showing that lipiodol has entered large branches of portal vein, and arterial bed is greatly increased (cf. fig. 3)

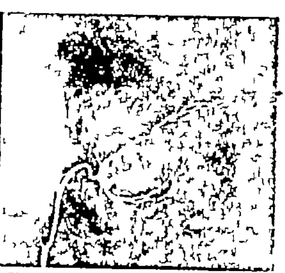

Fig. 3—Hepatic arteriogram (left lobe) in normal liver by same technique as in fig 2.

reach the deep aspect of the right rectus muscle a few centimetres from the xiphoid process was a large vein which was subsequently shown at necropsy to be the left para-umbilical vein. When the liver was retracted from the abdominal wall, the murmur could no longer be heard over the lower thoracic cage but it persisted unchanged in the vicinity of the xiphoid process and on both sides of the sternum It was promptly abolished in those latter areas when the vein in the falciform ligament was occluded by digital pressure The chest-piece of a sterile stethoscope was next applied to the postero inferior surface of the right lobe of the liver and of the quadrate lobe. A murmur was heard identical to but louder than that found on auscultation externally increasing in intensity as the porta hepatis was approached, and heard over the portal vein in the gastrohepatic omentum Light palpation of the portal vein revealed a purring thrill The hepatic artery was isolated and, when it was occluded by pressure between finger and thumb the external murmur and that over the liver and the portal vein promptly ceased. Occlusion of the portal vein did not exert any influence The spleen was removed. After the operation the patient developed an inexplicable peripheral circulatory failure which could not be corrected and he died six hours after the operation.

Necropsy Findings—The dilated collateral vein in the falciform ligament arose in the left branch of the portal vein and ran through the falciform ligament to the posterior aspect of the rectus sheath 3 cm. below the xiphoid process, where it divided into right and left branches, each branch anastomosing with the corresponding internal mammary vein. Incorporated in the wall of the vein close to its origin, but readily dissected from it was the ligamentum teres. The collateral was therefore a greatly dilated left para-umbilical vein. The liver was excised, Lipiodol was injected into the hepatic artery at a pressure of 50 mm. Hg; the liver was radiographed (fig 2) The lipiodol not only outlined the hepatic arterial tree but also entered large intrahepatic vessels in distribution corresponding to that of major branches of the portal vein The demonstration of lipiodol in the portal vein and its branches on dissection clearly established that these large vessels were branches of the portal vein. No lipiodol was demonstrated in the hepatic veins. Fig. 3 shows the hepatic arteriogram produced by the technique employed above in a normal liver excised at necropsy the lipiodol is confined to the arterial tree and does not enter the branches of the portal vein Comparison of figs. 2 and 3 shows a further significant difference: in fig 2 the arterial bed is greatly increased as a result of a great increase in the smaller branches of the hepatic artery The arteriogram in fig 2 might well be likened to a tree in summer and that in fig 3 the normal arteriogram, to one in winter

Direct Auscultation of Cirrhotic Livers

It seemed to us possible that in other cases of cirrhosis of the liver a hum of intrahepatic origin might be audible on direct auscultation of the liver when no hum was heard before laparotomy

9 consecutive cases of non alcoholic diffuse hepatic fibrosis have been investigated In none of these was a hum audible on auscultation before operation. However in 5 cases a continuous humming murmur was heard on auscultation of the postero inferior su of the right lobe and of the quadrate of the liver in each case becoming lo as the porta hepatis was approached 4 of these there was a systolic accentu and the hum was audible over the po vein, light palpation of which reveal purring thrill In all 5 cases the hum when present the thrill ceased when hepatic artery was occluded. In 3 of t cases a large left para umbilical vein demonstrated in the falciform ligam No hum was detected in the remainin of the 9 cases, nor in 10 subsequent ca with macroscopically normal livers, wi were similarly investigated

Discussion

The auscultatory findings at lap otomy and the hepatic arteriogram necropsy establish that the hum the present case had its origin in arteriovenous shu in the liver There is no reason to doubt that the h heard solely on direct auscultation of the liver in th cases of cirrhosis was of similar origin

The hum so produced seems to have been transmit to the parietes by two routes (1) along the large para umbilical vein to the neighbourhood of the xiph process, and thereafter for a short distance along internal mammary veins and (2) via the overly tissue. Since the hum was loudest in the vicinity of xiphoid process and was conducted to this area by collateral vein this mode of transmission seems to the more effective, but the presence of such a collate does not ensure conduction of the hum to the pariet as was seen in 3 of the 5 cases in which a hum was audi only on direct auscultation of the liver

According to Moschowitz (1948) arteriovenous shu in the cirrhotic liver were first demonstrated anatomica by Sabourin in 1885 an observation subsequently co firmed by Epplen (1922) and Popper et al. (1950) T histological observations of Cameron and Mayes (1930) the effects of experimental ligation of the hepatic arte in animals indicated the existence of communicatio between the hepatic artery and the portal vein arteriolar level in the normal liver and Wakim a Mann (1942) concluded, from observations on the tran illuminated liver of living animals, that interconnectio occurred between branches of the hepatic artery and the portal vein at sinusoidal and presinusoidal leve Herrick (1907) first noted the effects of these shunts arterial perfusion experiments on excised normal a cirrhotic livers He found that in normal livers there w a rise in portal pressure of 1 mm. Hg for every 40 mm. rise in arterial pressure, whereas in the cirrhotic liver was 1 mm Hg for every 6 mm Hg rise in arterial pressur Dock (1942) using kerosene as the perfusing fluid, showe that, if the portal vein and the hepatic artery wer perfused simultaneously at a pressure of 20 and 100 mm Hg respectively the rate of flow in the normal liv through the portal vein was 30% less than if the porta vein was perfused alone In contrast, he found that th rate of flow was reduced by 78% in alcoholic cirrhosi The perfusion experiments of Dock (1942) further showe that the degree to which arteriovenous shunts operate i cirrhosis varies widely, being in certain cases of non alcoholic cirrhosis less than in normal livers

Berman et al. (1951) and McFadzean and Cook (1953 have discussed the rôle played by arteriovenous shunt in the production of portal hypertension and, amon others have reported ligation of the hepatic artery i the treatment of portal hypertension This operation ca only be successful in the presence of excessive arterio venous shunting in the liver As emphasised b McFadzean and Cook (1953) where this is not present ligation of the hepatic artery may well lead to the removal of the main, or in some cases the only, blood-supply, with resulting ischæmic necrosis Such cases of necrosis have been recorded If it were possible to demonstrate active and excessive arteriovenous shunts, cases likely to benefit from ligation of the hepatic artery could be selected and those in which necrosis might occur could be excluded In view of the information obtained from hepatic arteriograms at necropsy hepatic arteriography at operation might prove of value, but our radiological facilities are inadequate for this purpose Observations on the influence of occlusion of the hepatic artery on portal pressure directly measured at operation are to be avoided because of a high incidence of portal-vein thrombosis in Hong-Kong Chinese suffering from diffuse hepatic fibrosis Since both these methods are denied us, the demonstration of a hum on direct auscultation of the liver may well prove to be of value in such a selection Although from a small series of cases it is impossible to draw general conclusions, it is of importance to note that 3 patients in whom a venous hum was heard over the liver at laparotomy had the hepatic artery tied and subsequently progressed satisfactorily, whereas 1 patient in whom no such hum was heard underwent the same operation and died from hepatic necrosis

The greatly increased arterial vascular bed seen in fig 2 is of great interest This increase has been found not only in other cases of diffuse hepatic fibrosis but also in biliary cirrhosis and primary carcinoma of the liver The full significance of this finding is under investigation and evidence is accumulating that suggests that the greatly increased arterial bed plays an important part in the genesis of ascites in these three conditions

Summary

In a case of diffuse hepatic fibrosis a venous hum was heard over a wide area A similar but louder hum was heard on direct auscultation of the liver at operation Occlusion of the hepatic artery abolished the hum Hepatic arteriography at necropsy showed numerous arteriovenous shunts between branches of the hepatic artery and of the portal vein, and it is concluded that these shunts were responsible for the hum

Direct auscultation of the liver at operation revealed a hum in 5 of 9 cases of diffuse hepatic fibrosis in which a hum was not heard previously In the absence of facilities for hepatic arteriography at operation a hum so demonstrated may aid selection of cases for treatment by ligation of the hepatic artery

A greatly increased arterial vascular bed was seen in the arteriogram of the case recorded This increase has been found not only in other cases of diffuse hepatic fibrosis but also in biliary cirrhosis and in carcinoma of the liver

We wish to thank Prof Hou Pao Chang, of the department of pathology, University of Hong Kong, and Dr H. C Ho, senior radiologist, Queen Mary Hospital, for their coöperation.

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RIGHT-SIDED THORACIC APPROACH FOR COMBINED LOBECTOMY AND MITRAL VALVOTOMY

K M SHAW
M B Dubl, F R C S I

LATE SURGICAL FIRST ASSISTANT, LONDON CHEST HOSPITAL

THE operation of mitral valvotomy for mitral stenosis has rapidly become established as a routine procedure with a standardised technique The early approach through an anterior thoracotomy with the patient supine has been largely abandoned in favour of the more direct posterolateral thoracotomy through the left pleural space, with the patient in the right lateral position. The pericardium is opened widely, and the mitral valve is approached through an incision in the auricle of the left atrium

So far as I can ascertain, no report has been published of an approach to the mitral valve through the right pleural cavity It is easy to conceive of a situation where such an approach would be advantageous, as in the following case

CASE-REPORT

The patient, a small frail woman aged 52, presented with cough and pain in the chest and was found to have an undifferentiated carcinoma of the lower lobe of her right lung. Preoperative examination revealed mitral stenosis, although she had previously been in good health with no symptoms of heart disease This was confirmed by a cardiologist, who found the heart slightly enlarged, with evidence of right ventricular hypertrophy, the heart was in regular rhythm, and there was no evidence of congestive failure He agreed that thoracotomy was justifiable after preliminary digitalisation

Operation —A right posterolateral thoracotomy was done through the bed of the fifth rib, with the patient in the lateral position There were no obviously invaded hilar glands, and lower and middle lobectomy was done without difficulty The patient's general condition had given some anxiety from the induction of anæsthesia, and during the pulmonary resection auricular fibrillation began It was thought that recovery might be facilitated if the mitral stenosis could be relieved. The pericardium was opened round the stump of the inferior pulmonary vein, and a clamp was placed on the left auricle at the base of the vein, from which the ligature was then removed The tip of the right index finger was next inserted into the vein, and the clamp removed The lumen had to be stretched considerably before the finger could be wholly inserted into the auricle There was slight regurgitation *from the mitral orifice, which was as large as the finger tip* The commissures were easily split to admit the finger The posteromedial commissure was split further, but on the attempt to split the anterolateral commissure further the valve moved away to the left before the finger, and no purchase could be obtained The final aperture was estimated to admit two fingers On removal of the finger the clamp was replaced on the auricle and the vein closed with a continuous fine silk suture The chest was closed in routine fashion with drainage, and the patient's condition was much improved at the end of the operation

Pathology —Section of the growth confirmed the diagnosis of undifferentiated carcinoma without evidence of gland invasion

Convalescence was uneventful, the patient being up on the fourth and discharged on the sixteenth postoperative day She was examined by a cardiologist before discharge, and it was considered that the signs of mitral stenosis were less evident than before the operation There were a slapping first sound and only a faint diastolic murmur, auricular fibrillation was still present

COMMENT

Mitral valvotomy through the right inferior pulmonary vein after lobectomy is feasible and technically simple, providing finger pressure is sufficient to separate the fused commissures

This patient was under the care of Mr J R Belcher, to whom my thanks are due for permission to publish her case-record

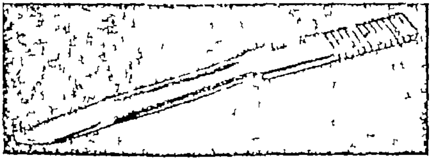
New Inventions

ELEVATORS TRANSPARENT TO X RAYS FOR SMITH-PETERSEN NAILING OPERATIONS

A DISADVANTAGE common to bone elevators or xtractors normally used during operations for insertion f Smith Petersen nails and allied procedures under X ray control is that they have to be removed each time adiographs are taken, or else they may spoil the ilm.

Trauma and time may be spared by using elevators hat may be left in situ throughout the operation

The type shown here is not unlike the Bristow bone ever, but the shape may be altered when necessary to enable it to remain in the wound when films are being taken The material used is polymethyl methacrylate * (unplasticised) having the following qualities it can be sterilised by boiling it is slightly malleable when very hot, and it resumes its original shape after boiling



These elevators are made by Allen & Hanburys Ltd., 48 Wigmore Street London, W 1,

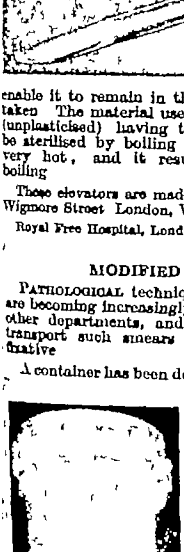
Royal Free Hospital, London

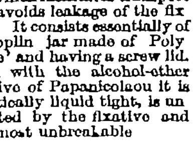
ROY H MAUDSLEY
F.R.C.S

MODIFIED "COPLIN JAR

PATHOLOGICAL techniques involving wet-fixed smears are becoming increasingly common in gynæcological and other departments, and it is sometimes necessary to transport such smears while still immersed in their fixative

A container has been devised which facilitates transport and avoids leakage of the fixative It consists essentially of a 'Coplin jar made of Polythene' and having a screw lid. Used with the alcohol-ether fixative of Papanicolaou it is practically liquid tight, is unaffected by the fixative and is almost unbreakable





The design was submitted to A. R. Horwell 18 Christchurch Avenue, London, N W 6 who has arranged for its manufacture.

Imperial Cancer Research Fund
Laboratories,
Royal College of Surgeons of England,
London

STRETTON YOUNG
M.B St. And.

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* Made by Imperial Chemical Industries Ltd. under the trade name Perspex.'

Reviews of Books

Social Medicine

S LEFF, M.D, D P H., barrister-at-law London Routledge & Kegan Paul. 1953. Pp 297 28s.

SINCE the Goodenough report et al., it has been fashionable at medical hunt breakfasts for the Master in the Leacockian manner, to stride to the sideboard drain a dipper of Social Medicine, and gallop off in all directions. The dust wrapper of Dr Leff's book promises us "a completely new approach to the subject,' but it is in fact a forcible and well-documented plea for more attention to be paid to social factors in health and disease and as such is in the direct and grand tradition of Chadwick, Southwood Smith, Farr, Simon, Ryle, and Winslow This is by no means to say that it was not needed and need not be read

After discussing (but failing to define) social medicine Dr Leff relates his subject to the background of history, and sets out his thesis that the most promising field of advance in medicine today is by the application of social measures *This he illustrates by chapters on the infectious diseases* death rates, housing nutrition working conditions tuberculosis, rheumatism, mental disorder the aged war, and the health services. It is not a textbook, but special pleading of a high order The sections on the results of statistical research, on conditions of work on mental disorders, and on the effects of atomic explosions are particularly good. Perhaps the most valuable is that on the health services which includes an attack on excessive specialisation His illustrations of the economy resulting from preventive programmes may be commended to ministers of health in all countries. 'The question is not whether we can afford to carry out these social reforms, but whether we can afford *not* to carry them out.' Dr Leff is convinced that medicine is facing a crisis (it always is, of course), and that social medicine is one of our main weapons in the battle against disease, both in the struggle for the elimination of adverse social factors and for the advancement of the theory and *practice of medicine. It is the medicine of the future* emerging from the medicine of today" Whether we go the whole way with him or not, this book can profitably be read by all concerned with the future of medicine

Hormonal and Neurogenic Cardiovascular Disorders

Endocrine and Neuro-Endocrine Factors in Pathogenesis and Treatment. WILHELM RAAB M.D. F.A.C.P F.A C.C F C.C.P professor of experimental medicine and head of cardiovascular research unit, University of Vermont. Baltimore: Williams & Wilkins London Baillière Tindall & Cox. 1953 Pp 722. 114s

As Professor Raab points out, it is one thing to admit the existence of certain facts and another to incorporate them as tools into one's daily reasoning In writing this book, however he has clearly carried the process a long way In the first section he surveys the effects of individual hormones, such as thyroid, pituitary extract noradrenaline and adrenaline, on the cardiovascular system. In the second he recounts the cardiac manifestations of the differing endocrine syndromes, including phæochromocytomas In the third section he discusses the influence of hormonal and endocrine effects on various cardiovascular syndromes, such as angina pectoris and congestive cardiac failure His intention has been to struggle out of the dead end street of exclusively mechanistic thinking in matters of cardiovascular pathology and therapy ' In this he is right for little more can be deduced about the fundamental causes of heart-disease from hæmodynamic and electrocardiographic observations: advance now depends on study of the profound metabolic upsets seen in congestive failure, the severe cardiovascular disturbances in endocrine disorders, such as phæochromocytoma, and the fundamental changes wrought by corticoid therapy In particular he has been concerned with the possible rôles of noradrenaline and adrenaline and the ways in which *they are inactivated* or potentiated by abnormal states in the body, with consequent effects on the cardiovascular system. It is a little difficult to accept some of his arguments, many of which are based on biochemical measurements which are not yet sufficiently accurate This does not in any way deny the force of his general theme, in support of which he has provided a complete review of all the non-mechanistic factors affecting the heart Few important references can have been omitted from the 3700 he supplies, of which more than 70 apply to his own work Though his English at times is difficult to follow, all cardiologists should read this book

Ear, Nose and Throat Diseases for Medical Students

WILLIAM MCKENZIE, M B Camb, F.R C S, surgeon, Royal National Throat, Nose and Ear Hospital Edinburgh E & S Livingstone 1953 Pp 256 21*s*

THERE are two features of this new book that will immediately commend it to the medical student—its size and its price There are also many good things in it—pleasant production, a useful list of E N T questions set in the qualifying examinations of London University and the Conjoint Board, brief illustrative case-reports, and some good photographs of the methods of clinical examination But there is far too little on the basic sciences, the important subject of cancer is dismissed in the short space of 11 pages, much of which is devoted to photographs of advanced cases, while early symptoms are inadequately described, no description or illustrations of tracheotomy tubes are given in an otherwise good description of the operation, and one statement in particular is a dangerous exaggeration —that "a careful history is more important than any examination by special instruments"

A Dictionary of Midwifery and Public Health

G B CARTER, B SC, S.R N, S C M, M T D, and G H. DODDS, M D, F R C S, F.R.C O G London: Faber & Faber 1953 Pp 686 25*s*

Miss Carter and Miss Dodds have written this book primarily for midwives, but they hope—and on good grounds—that it will be of use to other workers in the public-health field, and also to medical students It is much more than a dictionary of terms, though it is that too, but the definitions are supported by explanations, so that it has more of the nature of an encyclopædia than a dictionary (and indeed it is the offspring of an earlier work, the *Midwife's Dictionary and Encyclopædia*)

Thus the entry headed "hæmolytic disease of the newborn" is a little article filling 5¹/₂ columns of text, giving a clear and up to date summary of rhesus sensitivity, types of hæmolytic disease, prophylaxis and treatment, and ending with a cross-reference to "rhesus blood groups" In the same way, "uterine inertia" is dealt with in an informative and practical article of 7 columns, and the same principle holds throughout the book It has evidently been put together with great care and labour, and the terse clear sentences are a pleasure to read Occasional line drawings, equally clear and economical, illustrate the text The section on public health and administration occupies some 130 pages at the end of the book, and deals mainly with those aspects of public health which affect pregnant women, infants, and growing children

The Breast in Roentgen Diagnosis

RAUL A LEBORGNE, M D, head of the radiologic department, instituto de Radiologia y Centro de Lucha Contra el Cancer—Hospital Pereira Rossell, Montevideo, Uruguay Translated by Lucy Crocker de Leborgne Montevideo Impresora Uruguaya, S A London Constable Pp 194. 63*s*

IN this country radiography has not so far been found a useful means of diagnosing breast lesions Dr Leborgne's book suggests that this may perhaps be the result of insufficient attention to technique It consists largely of X-ray pictures, supported by photographs of specimens and slides, and makes a good case for a much more thorough trial of radiography in this field He finds straight radiographs of the breast the most generally useful, particularly for neoplasms in the breast substance Contrast radiography, after injection of the ducts with a dir opaque medium, is employed for the diagnosis of duct lesions, particularly of those which produce a nipple discharge without other clinical signs

In a short opening chapter on technique he describes intraductal biopsy by means of fine wire loops introduced into the duct openings after they have been dilated with a small laminaria tent, this is the sole example in which technical virtuosity seems to outrun utility Normal radiological appearances are discussed in the second chapter The secreting and fibrous tissue of the breast are more opaque than the surrounding fat, and the value of straight radiographs depends on this fact In young women, especially when they are lactating, the predominance of secreting tissue makes radiology less useful than it is when advancing age has brought infiltrations of fat The third and longest chapter deals with carcinoma of the breast Malignant tumours show up as opaque masses with a spiculated edge and thickening of the neighbouring ligaments of Cooper—points which are well seen in the illustrations, and contrast strikingly with the smooth edge of benign tumours and cysts. Thickening of the skin over malignant tumours may also be seen, and a characteristic spotty calcification is sometimes apparent, especially in duct carcinomata Short chapters on cystic disease, fibro adenoma, infective mastitis, and certain rare conditions occupy the rest of the book

Dr Leborgne has found an able translator in his wife, who writes proper English prose, with only an occasional word to which we are not yet accustomed The 307 photographs and diagrams, all in black and white, are well reproduced

Atlas of Medical Mycology

EMMA SADLER MOSS, M.D, director, department of pathology, Charity Hospital of Louisiana, New Orleans, and ALBERT LOUIS MCQUOWN, M D, pathologist, Our Lady of the Lake Sanitarium, Baton Rouge, Louisiana. London Baillière, Tindall, & Cox 1953 Pp 24, 61*s* 6*d*

AN atlas of medical mycology should not be merely an illustrated textbook, and it cannot be a substitute for a textbook Special care is required in the selection of the illustrations to ensure that they fulfil the peculiar purpose of the atlas, showing clearly the characteristic features of the subject, whether clinical, pathological, or mycological In some instances, coloured reproductions may be necessary

In this work the authors have presented a collection rather than a selection of photographs, and though some are good others are disappointing, and a few could be identified only by reference to the legend The general plan of the book is sound, and with better illustrations it should make a valuable atlas

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Textbook of Pathology (6th ed. London Henry Kimpton. 1953 Pp 1024 88*s*)—"In 1951," says Prof. William Boyd in the preface to the sixth edition of his well-known textbook, "over 73,000,000 pounds of synthetic chemicals were administered with or without good reason in the United States, or half a pound for every man, woman and child in the country", and he mentions in passing that the wholesale change in the normal bacterial flora of the bowel produced by antibiotics "may have dangerous or even fatal consequences." As the author of a text on pathology he has his own reasons for feeling testy about the modern appetite for drugs diseases which were formerly common and fatal have disappeared or become relatively trivial, and new diseases have appeared in their wake, and it all makes a lot of work But a man who produces a large textbook and then revises it six times in 20 years is a glutton for work in any case, and his stupefying list of new material suggests that no student need fear (or hope) that he has left anything out

An Atlas of the Commoner Skin Diseases (4th ed. Bristol John Wright London Simpkin Marshall. 1953 Pp 371 75*s*)—Dr Henry Semon's admirably illustrated book has for nearly twenty years been giving a very helpful hand to those who find skin conditions a recurrent cause of perplexity A number of new photographs have been added in this latest edition, but the majority are those originally prepared under the direction of Dr Semon's collaborator, the late Dr Arnold Moritz They will long stand as a tribute to his outstanding skill at this work.

THE LANCET

LONDON SATURDAY, NOV 28 1953

Operating-theatre Infections

DESPITE the aseptic ritual of even a well run operating theatre, surgical wounds are probably contaminated more often than the surgeon believes The contamination is seldom clinically significant, however either because the organisms introduced are not pathogens or because they are not too many for the tissues readily to destroy them The skill of modern operating and the efficacy of chemotherapy have further reduced the risks of minor contamination of deliberate wounds This means however, that the postoperative infections which still supervene are more likely to have such tragic consequences as those described in two recent reports. One of these recounts the death of an 18 year old girl from tetanus after appendicectomy [1] The other, to which Dr SEVITT refers in his article on an earlier page, concerns a man of 26 who fractured and dislocated his left ankle at football, and lost his leg above the knee because gas-gangrene caused by *Clostridium welchii* followed an open operation on the ankle The source of the girl s infection was not settled but Dr SEVITT's inquiries into the case of the young footballer leave little doubt that the infection resulted from the exhaust system of ventilating the operating theatre This conclusion is strengthened by the evidence in SEVITT s earlier report [2] that the same ventilation plant, by causing aerial dissemination of tetanus spores, was responsible for two cases of postoperative tetanus, one of them fatal In 1946 ROBINSON et al [3] reporting two fatal cases of postoperative tetanus, emphasised the need to exclude infected dust from operating theatres

What can surgeons do to eliminate this small but deadly residue of postoperative infections? However many of the details of sterilisation they must inevitably delegate to theatre-sisters and staff nurses, they should satisfy themselves about the measures taken in their theatres to ensure the sterility of gowns masks, swabs packs, dressings gloves, talc penicillin and other powders solutions lotions local anaesthetics, syringes, and so forth The measures must be adequate in the first place and the understanding and efficiency of those who carry them out ought to be checked periodically In particular it is essential to make sure that the theatre autoclave is used properly If drums are too tightly packed, or if a proper vacuum is not established and maintained before turning on the pressure, the temperature needed for sterilisation may not be reached in all the material within the steriliser This point can be simply checked by including in the steriliser, and later submitting to the laboratory for culture a suitably wrapped test swab which has first been contaminated with dust known to contain sporing organisms From the accidents already cited, it is evident that surgeons should al look into the possibility of dust being disseminated l the ventilating system of their theatres As D SEVITT emphasises, the real villain of the piece is th exhaust type of ventilation which sucks air and du from the hospital and theatre corridors and from oth parts of the hospital, into the operating theatre, that the theatre becomes an " air sewer " draining in itself dust often contaminated with sporing organism Upward draughts towards the vents suck floor du into the air and every wound in such a theatre exposed to serious risk of dangerous contaminatio BOURDILLON and COLEBROOK [4] devised a speci dressing unit with a system of ventilation whic delivers filtered warmed, and humidified air from th ceiling The air, which is extracted at floor level, changed 10–20 times per hour without discomfort occupants of the room. This plant is expensive put in and to run, but it should be at the very least guide to the design of the ventilation for futu operating theatres, and its costs must be measure against the disasters caused by a method of ventilatio now clearly and tragically established as dangerou Until a completely satisfactory system of ventilatio can be installed in all theatres there is need to reduc the dangers from existing conditions Operatin theatre floors and walls should be regularly dust with damp cloths wrung out of antiseptic solutions precautions should be taken against introduction infected dust on the footwear of those coming into th theatre preferably by their putting on gumboots some equivalent which have been left standing in stron antiseptic and hospital corridors and blankets shoul be oiled to reduce dust dissemination in hospital But perhaps the most important thing is to tackle th present exhaust systems of theatre ventilation. F example it has been suggested [5] that extractor fa may be reversed so that they draw air into the theat through their ducts, which can readily be guarded b fitting them with air filters This produces a outward draught of air through the doors of th theatre into the hospital corridors Such a relativel uncontrolled method of disposing of warm air an steam from the theatre is not ideal, but it would no be a bad thing perhaps if the unpleasant visibl consequences of its use drew attention to the need for proper system of theatre ventilation It is better t accept the disadvantages of this simple expedien than to tolerate unmodified a system which has bee proved dangerous to the lives of patients

Civilised—and Sedentary

OCCLUSIVE coronary heart-disease is often regarde as one of the disorders of civilisation. Its appare predilection for the medical profession has led to it being called the doctors disease with the flatterin suggestion that doctors are particularly civilise A popular view is that the greater prevalence of th and some other conditions reflects the greater stres of modern life In a sense this is a truism an rapid increase in incidence is likely to depend o environmental changes, and any disease provokin change may reasonably be called a stress. Bu those who use the phrase are probably thinking mor generally in some way, they imply, we get a tougher break from life than our ancestors did

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[1] *Middlesex Advertiser* Sept. 25 1953

[2] Sevitt, S. *Lancet*, 1949 ii, 1075

[3] Robinson, D T., McLeod, J W Downie A. W *Ibid*, 1946 i, 152

[4] Bourdillon R. B., Colebrook, L. *Ibid*, pp 561 601.

[5] *Army med Dep Bull.* 1941-4 [illegible] p [illegible]

The increase in occlusive coronary heart-disease is real, if hard to estimate MORRIS[1] has pointed out that, though better diagnosis and treatment should have reduced deaths from (for example) cardiac rupture these are in fact becoming more frequent On the other hand he showed that severe atheroma is, in contrast, becoming less common This suggests that occlusion is a complication and not an integral feature of atheroma , and we should therefore separate the two problems—the cause of atheroma, and the cause of thrombosis (or other occluding process) in atheromatous vessels Much work, mostly American, on the first problem has produced a strong case for regarding atheroma as a sequel of disordered lipoid handling[2] Broadly speaking, the suggestion is that the arteries are not quite watertight, that there is continual leakage of plasma into the venæ vasorum and adventitial lymphatics, and that the less soluble lipoid *moieties of lipoprotein complexes will tend to* be sieved out in the intima The outward flux will be greater where the blood-pressure is higher, and lipoid trapping will be assisted by endothelial thickening or local lymphatic obstruction This would explain the concentration of atheroma in the lower aorta or over regions of aortitis, and its occurrence in the pulmonary artery only when the pressure there is raised But the most important variable, it is thought, is the state of the plasma-lipoids The concept is that each individual consuming a given number of calories can safely handle a certain quantity of dietary cholesterol (mostly from eggs and other dairy produce) , but, if this is exceeded, the normal lipoid transport will be overloaded and a more "atheromagenic" type of lipoprotein will appear in the blood The dietary cholesterol threshold is probably lowered by an excess of total calories and also by such diseases as hypothyroidism and diabetes Whether right or wrong these views are more likely to stimulate therapeutic research than the picture normally offered to British students of an inevitable furring of the pipes with age As the dangerous foods are expensive in peace and scarce in war, a greater prevalence in the well-to-do and a decrease during rationing periods are to be expected

In an article concluded in this week's issue Dr MORRIS and his colleagues produce important new evidence about the incidence of occlusive disease By comparison between occupations within the same social group but involving different grades of physical exertion, they show that the disease is commoner in the more sedentary workers It is also more severe more die in the first occlusive attack and fewer escape major infarction to present as angina of effort Does this greater prevalence among the sedentary reflect more atheroma or some other factor favouring occlusion in atheroma ? If the former, is there a difference in eating habits between the active and sedentary workers ? This seems unlikely, but a sample comparison would be worth making The more general findings of MORRIS and HEADLY[3] may provide a clue They found that sedentary workers show an excess of deaths from quite a number of disorders (including appendicitis, diabetes, and duodenal ulcer) which have been regarded as diseases of modern life

If *the excess of coronary disease in light* workers is not due to more atheroma, our tentative conclusion must be that, while atheroma follows faulty diet, the likelihood of occlusion is increased by sedentary habits It will be interesting to see how readily these notions are accepted by the profession Doctors who smoke have been moved to unparalleled subtleties of statistical exegesis in their efforts to prove that the cause of the commonest cancer has not been discovered Will they welcome the idea that the stresses of modern life that give them coronary disease are the outcome of unwise eating and deficiency of exercise ?

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[1] Morris, J N *Lancet* 1951 i 1 69

[2] Allen E V Katz, L N Keys A Gofman J W *Circulation* 1952 5 95

[3] Morris J N Headly, J A. *Brit J industr Med* 1953, 10 245

Mumps Sensitivity Tests

ALTHOUGH typical cases of mumps with involvement of the salivary glands may be diagnosed readily enough, there are circumstances in which immunological tests of infection or resistance to infection are of value During attacks of mumps and the subsequent convalescence, specific antibodies to the virus appear in the serum and are detectable by complement fixation methods[1] Using the allantoic fluid from fertile eggs infected with mumps virus, two antigens participating in the complement fixation reaction have been prepared[2] One of these, designated S, is regarded as the soluble antigen and is obtained from the supernatant fluids, whilst the other, the V antigen, is associated with the virus bodies themselves During an attack of mumps, antibodies to the S antigen appear in the blood before V antibodies , and, since S antibodies appear within a week of infection,[3] their presence in the serum is a help in early diagnosis, Antibodies to the S and V antigens persist in the blood for 9–18 months, and when they are detected a mumps infection within this period can be presumed The mumps virus agglutinates human and chicken erythrocytes, and in cases of mumps the serum contains antibodies inhibiting the hæmagglutinin[4] The antihæmagglutinins appear in the blood-stream soon after the complement-fixing antibodies, but the value of the test is limited by the instability of the antigen used for the test

After a patient has recovered from mumps his skin is hypersensitive to inactivated mumps virus, and this reaction is apparently unrelated to the development of complement-fixation antibodies For the skin test, the virus used has been obtained either from the parotid glands of infected rhesus monkeys or from infected fertile eggs , and it has been inactivated by heating or by treatment with formalin[5] On another page of this issue Professor CHOREMIS and his colleagues in Athens report that the cerebrospinal fluid of patients with mumps meningitis can be used as the source of antigen for skin-testing The heated centrifuged deposit from cerebrospinal fluids taken on the fifth day of the disease was found to produce skin reactions in patients with mumps and in those who had lately recovered from the infection. Positive skin reactions were obtained in 90% of the children who had had mumps within the previous six months, but in only 74% of those whose attack had been between six and twelve months previously

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[1] Enders J F Cohen S , Kane, L W *J exp Med.* 1945 81, 119

[2] Henle G Harris, S Henle W *Ibid*, 1948 88 133

[3] Ray B G Swain H A. *Brit J exp Path* 1953, 12, 501

[4] Robbins F C Kilham, L , Levens, J H , Enders, J F *J Immunol.* 1949, 61 235

[5] Enders J F , Kane L W , Maris, E P , Stokes J jun. *J exp Med.* 1946, 84, 341

The hypersensitivity shown by the skin reaction is evidence of resistance to mumps following previous infection and it is therefore of value in excluding the possibility of the disease developing in these people when they have been exposed to infection [6] The test is also useful in implicating the mumps virus as the cause of an orchitis or a meningitis, when the hyper sensitivity develops two or three months after the infection A considerable proportion of patients with mumps show some involvement of the nervous system and in some cases there may be meningo-encephalitis without swelling of the salivary glands Although the skin tests or serological reactions are clearly of value when used in this way, there has lately been a tendency to discourage tests of skin hypersensitivity, because the reaction may be late in appearing and because the material injected may itself stimulate the production of complement-fixing antibodies in non infected persons

Epidemiology of Influenza

INFLUENZA viruses, and particularly influenza A viruses, are notoriously variable in their antigenic characters, and there are two views about the pattern of their variability Some virologists believe in continued antigenic novelty they consider that the antigens are undergoing progressive modification from one epidemic to the next older antigens being gradually replaced by newer ones every few years Others think that the influenza viruses contain a finite number of antigenic components, which undergo quantitative changes or rearrangements within the virus particle from one epidemic to another and Prof T FRANCIS of Ann Arbor speaking last week to the section of epidemiology of the Royal Society of Medicine, made it clear that he belonged to this second school. A decision between these two possibilities has practical significance, for it would determine policy in the use of influenza vaccines. If there are a finite number of virus antigens, it is conceivable that the antigenic changes will pursue a circular course, and we may be confronted once more with the influenza viruses of two or three decades ago With this possibility in mind, Professor FRANCIS would advocate including early as well as recent strains of influenza virus in current vaccines. Two types of investigation in his laboratory have a bearing on this viewpoint. The first is a study, with virus-absorbed antisera, of representative strains of influenza virus recovered during the past twenty years Among the strains examined a number of antigens could be identified, and there was clear evidence (as in other studies [7]) of the gradual appearance and disappearance of antigenic components. Recently isolated strains were far removed antigenically from the strains of twenty years ago, but some strains recovered in 1947 were intermediate in character between older and more recent strains Until now the change has appear be unidirectional. The second investigation was cerned with antibodies against representative influ strains, of the last two decades, in some 2000 speci of sera taken from people of different ages Prof FRANCIS found that children's sera showed anti against recently isolated strains only, while sera older people showed antibody mainly against viruses prevalent at the time when they might first contracted influenza This interesting and u pected finding falls into line with the studies on antigenic characters of the viruses, but it also sugg that people tend to respond to infection with influ virus by producing more antibody against the st of virus which first attacked them rather antibody against the current strain The implicat of this finding in relation to influenza immu both natural and artificial will require car evaluation

Another conclusion from this work is that viruses of swine influenza which are antigenica related to earlier strains of human influenza A w prevalent at the time of the 1918–19 influenza p demic ANDREWES et al [8] found in 1935 that s from children under 10 unlike sera from adu contained antibody against human but not sw influenza virus, and, basing his view on this obser tion, LAIDLAW [9] suggested that the virus of sw influenza became established in swine during 1918–19 pandemic STUART HARRIS et al [10] tested s from St Helena which had escaped the pandem the islanders had low levels of antibody to the sw virus but, after a mild influenza epidemic th in 1936 antibodies appeared in the sera of a numb of them. The conclusion was that the swine influen antibodies might merely represent a broad antiger response to a related virus, and there was experiment evidence of the ferret's immunological response infection to support this belief Professor FRANCIS results support the alternative interpretation th swine-influenza viruses were prevalent during the fe years before and after the 1918–19 pandemic and th a highly virulent mutant of that antigenic make-u was responsible for the pandemic On this hypothes the St Helena population might have been infecte earlier with a less virulent strain of the swine-influenz type

At the same meeting Prof. C H STUART HARRI described the investigation which he and his colleagu carried out during last winter's influenza outbrea in New York State Sera were collected at interval from a number of districts in different parts [illegible] State, and they were tested for evidence of [illegible] infection by the complement-fixation test [illegible] antigen In this test a positive result [illegible] indicate recent infection, since complement-fixing antibody, unlike neutralising [illegible] to disappear fairly rapidly after infection [illegible] areas investigated, influenza was not [illegible] winter but reports were received from [illegible] of increased numbers of cases during February and March. This peak coincided with [illegible] in the numb of positive sera which [illegible] from about

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Cabasso, V J., Hoagland, R. J J Amer med Ass 1953 152 1517

Hirst, G. K. J exp Med. 1952 96 589

8 Andrewes, C. H., Laidlaw P P, [illegible] Brit J [illegible] 1933 14, 466.

9 Laidlaw P P Lancet [illegible]

10 Stuart Harris C. H., Andrewes C. H., [illegible] Ser med Res Coun [illegible]

during December and January to about 15–20% of the samples tested during February and March, and in the following months this proportion declined considerably In further investigations of this type it would be necessary to show that samples taken in the preceding summer had practically no antibody Meanwhile, these results suggest that there may be a wide seeding of virus in the form of subclinical infections a month or two before an actual outbreak As Professor STUART-HARRIS remarked, there may be a connection between these results and ANDREWES's postulated "basic" inter-epidemic virus[11], and this is clearly a point worth investigating

In the search for influenza virus in subclinical infections, it would be important to have a screening test for determining which washings or garglings are likely to yield virus The nasal-inhibitor test of FAZEKAS DE ST GROTH[12] would be suitable for this purpose, but Dr B E ANDREWS told the meeting that technical difficulties in its application necessitated further investigations He described the laboratory tests and Dr J C MACDONALD the clinical examinations made during a vaccination experiment in a Luton factory last winter They were encouraged to find good agreement between clinical and laboratory tests in most cases In addition to the influenza A one case of influenza C was suspected on serological grounds, if confirmed this would be the first case reported in this country

The news and views put before this meeting prompted Dr F O MACCALLUM to remark that though it was twenty years since the influenza virus was first recovered in the laboratory, this field of research had lost none of its life And it was encouraging to note that many laboratories in this country are hard at work, either on their own account or as part of the international programme of research organised by the World Health Organisation A report,[13] lately published in Geneva, shows clearly the extent of last year's world-wide influenza epidemic and illustrates in vivid terms the size of the problem. The influenza virus intends to keep us busy for some time to come

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[11] Andrewes C H *Proc R Soc Med* 1942 36, 1

[12] Fazekas de St Groth S *J Hyg Camb* 1952, 50, 47

[13] *Epidem Vital Statist Rep* 1953, 6, 203

Annotations

COUNTER-ATTACK ON SMOG

To say that every day tons of soot and grit fall on our industrial towns is not a pleasantry but a fact In 1950–51 the London County Council placed collecting-trays at four points in mixed residential and industrial districts, and other trays in the neighbourhood of power-stations The average deposit in the first four areas was found to amount to about 1 ton per sq mile per day which seems plenty, until it is realised that in the neighbourhood of power stations the figures ranged from 1 to 79 tons per sq mile in summer and from 4 to 72 tons in winter The three power-stations of Fulham, Lots Road, and Battersea lie within a circle with a radius of a mile, and their coal consumption is nearly 2,000,000 tons a year There was a time when it was the boast of employees at one of these great power-stations that a white plume about a yard long was all that anyone could see coming from the noble chimneys Now the picture has changed to that described by Dr Horace Joules in a recent letter[1] The London County Council, in a statement of evidence[2] to be submitted to the committee now inquiring into the causes and effects of air pollution (the Beaver Committee), say that when a power-station is to be built they have always pressed for the installation of the most efficient means of preventing the discharge of soot, ash, grit, and gritty particles, and that they have also pressed for remedial equipment to be installed in the older power-stations, to mitigate the nuisance The failure of their efforts to change the face of London they attribute in part to the difficulties arising from the use of coal containing a higher proportion of ash than the grit arrestors can cope with However it may be with power stations, Mr John Fox, in the current issue of *Smokeless Air*,[3] claims that steam raising factories can burn low grade fuel—and even the reviled "nutty slack"—efficiently and without smoke, provided they install suitable stoking equipment Such equipment is expensive, and he regrets that combustion equipment has been specifically excluded from the Government's loan scheme for increasing industrial efficiency

Power stations and industrial firms contribute only half our smoke domestic fires provide the other half. Here the use of smokeless fuels should help, but it offers no complete or immediate answer As the Earl of Selkirk[4] pointed out in the recent debate in the House of Lords, less than 1 million tons of smokeless fuels are put on the domestic market every year, as against 35 million tons of coal and 3 million tons of coke. We should get less smoke if householders used coke for heating, but coke cannot be burned in the old fashioned grates which are still the commonest types, and smokeless fuels cost more than coal or coke The L C C suggest that the Government should do everything possible to ensure that ample supplies of smokeless fuel are made available at a competitive price Even that, however, would not rid our atmosphere of sulphur compounds

When coal is burned most of the sulphur goes up the chimney in the form of sulphur oxides, to be carried into our lungs on foggy days, dissolved in water vapour, as the most lethal components of fog and smog In big plants the sulphur compounds can be very largely removed from flue-gases by washing, but this process costs 8–10s per ton of coal burned The flue-gas washing plant at Fulham power-station was allowed to go out of use during the war and has not been reinstated. Because of the difficulties of keeping such plants in operation, and the high cost of the process, flue gas washing, the L C C say, is not economically practicable for ordinary industrial firms Even for power stations it may have its drawbacks the British Electricity Authority argue that the discharge of hot gases from high chimneys is likely to ensure much wider (and therefore less harmful) dispersal of sulphur compounds than is the discharge of cool washed gases, and that when weather conditions favour fog, such washed gases are much more likely to hang about the power station and increase the percentage of sulphur oxides in the a than are gases carried off unwashed and piping ho On the other hand, it has been shown conclusively th gas-washing has reduced the concentration of sulph dioxide in the neighbourhood of Battersea pow station The L C C recommend the better clean of coal at the pits (which would remove some of sulphur compounds), and ask for power to sample fl s from shafts suspected of causing heavy pollution y also think powers for the establishment of smoke zones should be less cumbersome, and they urge need for speedy investigation of the many problems ch smoke abatement presents.

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[1] *Lancet* Nov 21 1953 p 1095

[2] Published in the L C C Agenda for Nov 17

[3] Autumn 1953 p 24

[4] *Hansard* 184, no 7 Wednesday, Nov 18

leanwhile, to citizens threatened with smog the long n preventive aspect appeals less perhaps than the k therapeutic measures proposed by Mr N Pilpel,[5] search scientist at King's College, London These e been submitted, on his behalf to the Beaver Com tee by the chairman of the scientific advisory council the Ministry of Supply Mr Pilpel suggests that y weak solutions of surface-active materials made with traces of 'seeding agents,' and sprayed finely n aircraft, could cause the water droplets of fogs to lesce and *fall as rain—carrying with them the soot,* and sulphur dioxide which they are supporting ding agents—such things as silver iodide, dry ice, l salt—spread, it seems, into cold clouds and drive supercooled water droplets together as snow but s only happens efficiently if the temperature is 10°C more below zero Since fog clouds are not cold enough respond in this way, Mr Pilpel suggests that such face-active *agents as the common soapless detergents* ld be used, either in conjunction with seeding agents separately They are already used in industry to rcome similar temperature difficulties The amounts ded would be so small that the cost of fog clearance uld be very low It all sounds too good to be true ence, however has now concentrated successfully almost every subject except ethics and the weather s may be an indication of an advance into new fields

THE E.E.G. AND THE MIND

THE relationship between electro encephalic changes d psychological disorders is far from clear Kennard[6] reviewed published reports with a view to answering ree questions (1) are abnormal E.E.G patterns mmon in patients with primary mental disorders who ve no other evident organic disorder of the nervous stem ? (2) to what factor or factors might such a fference be due ?; (3) of what significance is this fference ? Defining normality of the E.E.G is not sy, since some 15% of the 'normal' population have normal patterns. Even so, several studies have shown at E.E.G abnormalities are least common in groups ghly selected for fitness (such as R.A.F pilots) and r commoner in overt neurotics while they are most mmon in groups with known organic disease of the rvous system Attempts to correlate specific person lity patterns with specific E.E.G changes have proved rewarding A passive type of personality seems to be sociated particularly with alpha rhythm, and obsessive mpulsive features with paroxysmal dysrhythmia but his is of little diagnostic help in individual cases. The cords of psychotics are no more specific The one roup of patients with a characteristic E.E.G pattern re the aggressive psychopaths. Among children with haviour disorder E.E.G abnormality is even more usual han in adults with abnormal psychological traits.

Kennard concludes that the fluctuations of E.E.G attern may coincide with several different clinical ppearances on the one hand and with any one of several ifferent chemical or physical factors on the other No e factor has been shown to be of paramount importance, or is there any indication that the physical change is sponsible for the psychological change or vice versa ince E.E.G abnormality is commoner in people with sychological abnormality than in others its diagnostic alue may increase as methods become more refined ll that can be said at present is that instability of ersonality may be associated with instability of E.E.G pattern and the most obviously relevant E.E.G abnormality is a lowered threshold to environmental stimuli. This instability may arise from hereditary factors, changes in the structure or chemistry of the nervous system and possibly (and here is the difficulty) psychological factors.'

AUREOMYCIN IN THE PREVENTION OF RHEUMATIC FEVER

THREE out of every four children who are recovering from first attacks of rheumatic fever and who are subsequently untreated may be expected to have further attacks.[1] This recurrence rate is significantly reduced, however, if they are protected against respiratory infections with group A hæmolytic streptococci by effective and continuous chemoprophylaxis[2] The recommendations[3] of the American Heart Association's council suggest that for this purpose the drug of choice at present is sulphadiazine With daily doses of 0 5–1·0 g, given over long periods, toxic reactions are infrequent and usually slight, and a great deal of evidence is now available to show that this regimen may reduce the incidence of recurrent rheumatic attacks by as much as 90%[4] *If such a prophylactic scheme were widely applied* to those at risk in this country we could reasonably expect a considerable reduction in the number of cases of rheumatic fever But the occasional serious toxic effects of sulphadiazine and (perhaps more important) the emergence of significant numbers of resistant strains of streptococci must modify enthusiasm for the method

Penicillin, when wisely used against streptococcal sore throats, is of proved value in preventing rheumatic sequelæ[5] but evidence of its usefulness as a continuous prophylactic against incidental streptococcal infections is less convincing For this purpose, either oral or very long-acting parenteral preparations are essential, and, so far we have had insufficient experience of these kinds of penicillin to allow full assessment of their prophylactic value. Among the other antibiotics, aureomycin seems to be a possible alternative. McVay and Sprunt,[6] who have already used aureomycin continuously for long periods in patients with chronic infections have now given it a trial in the prophylaxis of rheumatic fever and they report favourably on the results. In their small series which consisted mainly of young rheumatic Negroes, observed over a period of nine months, the treated group received 500 mg of aureomycin daily No serious toxic effects were noted, and liver function tests *and bone marrow examinations were normal throughout.* The absence of gastro intestinal symptoms was attributed to the inclusion of the methyl and propyl esters of *p*-aminobenzoic acid in the aureomycin preparation—an addition which is said to discourage the development of moniliasis.[7] There was a significant reduction in respiratory infections and a lower recurrence rate in treated as compared with untreated patients

A comparison of the group A strains isolated serially from a group of non rheumatic patients receiving aureomycin with the strains from a control group showed no increase in the number of strains acquiring enhanced resistance to aureomycin This finding is perhaps less relevant than a consideration of the frequency of resistant strains in the general environment Strains relatively resistant to aureomycin certainly occur and may well become as common as sulphadiazine resistant strains.

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5. Times, Nov. 23, 1953
6. Kennard, M. A. *Psychosom. Med.* 1953 15 95

1 Hansen A E *J Pediat* 1940 28, 206.
2. Coburn, A. F Moore L. V *J clin. Invest.* 1939 18 147
3. See *Lancet*, 1953 i, 235 278
4. Dodge K G., Baldwin, J S., Weber M W *J Pediat.* 1944 483 Rheumatic Fever A Symposium, edited by Lewis Thomas. Minneapolis, 1952 p. 304
5 Denny F W Wannamaker L. W Brink, W R., Rammelkamp C. H., Custer E. A. *J Amer med. Ass.* 1950 143 151.
6 McVay L. V Sprunt D H. *New Engl. J Med.* 1953 249 387
7 McVay, L. V., Sprunt, D H. *Proc. Soc exp. Biol.* N Y 1951 78 759

Penicillin-resistant strains, however, are undoubtedly very rare, and this fact favours the further investigation of oral penicillin, rather than the expensive aureomycin, as an alternative to sulphadiazine

The results of McVay and Sprunt, therefore, do not suggest that, in the prophylaxis of rheumatic fever, aureomycin is likely to be superior to other bacteriostatic drugs, but it is probably an effective substitute in patients who are *intolerant to sulphadiazine or penicillin*

VISITING CHILDREN IN HOSPITAL

EMOTIONAL disturbances in children—bedwetting, temper tantrums, delinquency, and the like—date surprisingly often from a period in hospital, and there is good evidence that such disturbances are the outcome not of anything that happened to them in the wards, but of separation from the mother This evidence is so telling that in March of this year the Ministry of Health strongly urged all hospitals to allow daily visiting of children by their parents They were moved to take this step by the discovery that, in 1952, only 300 out of 1300 hospitals in the country which admit children allowed daily visiting, and that 150 prohibited it altogether[1] It is to be hoped that the figures are now very different, but it is disquieting to learn[2] that one management committee at least has rejected by 16 votes to 4 a resolution to introduce the daily visiting of children in hospitals in its group The chairman, who held that the committee should be guided by the strong request of the Ministry, noted at the outset that, though matrons collectively support daily visiting, doctors are collectively opposed to it Whether or not this generalisation holds elsewhere, it was certainly true at the meeting where the vote was taken No fewer than five doctors spoke against the resolution, most of them basing their objections on the sort of personal impressions which investigation has shown to be misleading Thus the experience of one had led him to believe that the daily visiting of children is not a good thing, he had seen, he said, too many emotional upsets in the ward and the outpatient department Another, who thought that the mother with a large family at home would find daily visiting a nightmare, was at once answered by a woman member of the committee such a mother, she said, can usually find someone to look after the family while she is away, and she added a simple statement of a complex psychological truth "If a child does not see its parents it grows away from them" Another doctor mistakenly argued that daily visiting is more for the sake of the parent than the child A fourth, who had been dumbfounded, he said, by the expressions of joy and happiness of children in hospital, had evidently been deceived by the superficial unconcern and cheerfulness which have misled so many The fifth doctor raised the practical objection that children of parents living near the hospital would be visited more often than those whose parents came from a distance, and that these latter would therefore feel neglected But if some must be deprived by circumstance, does it follow that the rest should be deprived by a hospital rule? That is an argument that could have some very odd conclusions

Some years ago we reported Miss Anna Freud[3] as saying in a memorable speech about the effect of hospital on the child

> "He lives from day to day, he depends on the evidence of his senses, and his understanding of the situation is fragmentary at best A loving mother who remains absent is a figure whom he is incapable of conceiving his own love demands the nearness of the beloved person, and if she withholds herself he lacks the only proof of love which he knows and can understand. His outward calm hides dejection and a feeling of having been abandoned by those he cares most about, he becomes inwardly apathetic, though capable of interest and animation on the surface. His roots in home are dying for lack of nourishment, and he is learning to do without them, at the expense of his normal emotional life and growth"

The child who is cheerful and unconcerned in hospital, and who takes his mother's coming and going without apparent perturbation, may be storing up trouble which becomes apparent only when he gets home The child who is disturbed by her visits and shrieks at her departure is in a far more healthy psychological state For such a child—or indeed for any child, as one member of the hospital management committee pointed out—the parting will be eased if he knows his mother will be back next day

It is interesting that another member of the committee, a woman, supported the chairman in his view that matrons—and nurses too, she said, as well as mothers and other women—are in favour of daily visiting At *one time some doctors held that the nursing staff would* never agree to daily visiting, but this, it seems, was probably a misplaced fear Having the child's ultimate *well-being in mind, they are ready to tolerate the tears*

THE CASE OF THE COUNTERFEIT JAW

IN the history of field anthropology there are a number of awkward discoveries which appear to fit nowhere into any coherent scheme of the relationships of man Prominent among these is the skull found some forty years ago at Piltdown in Sussex—a skull in which cranial fragments relatively modern in form appeared to be combined with a primitive mandible and dentition So peculiar was this combination felt to be that most anthropologists reserved judgment Evolution is not a tidy subject However, the lapse of time since the discovery of the skull has brought with it new methods of estimating the age of such specimens, and thus the chance of obtaining new information about the Piltdown fragments By a combination of fluorine analysis and estimation of the nitrogen-content Weiner, Oakley, and Le Gros Clark[1] claim to have shown that the mandible and teeth of the Piltdown discoveries are relatively modern, and cannot possibly be contemporary with the cranium But there is more than this Analysis has shown that the iron staining of the jaw, in contrast to that of the cranium, is only superficial, and that the coating on the canine tooth is a thin layer of "paint-like substance" It has also been shown experimentally that the morphology of the Piltdown teeth can be closely reproduced by artificially abrading the teeth of a chimpanzee

The suggestion is made, in round terms, that the mandible and teeth are part of a deliberate anthropological fake designed to mislead expert opinion. The evidence has not yet been discussed in full, but the preliminary report is damning enough If the skull is a fake, it has been a successful one From the pages of nearly every elementary book on our forefathers there peers a truculent hairy creature bearing the legend Piltdown Man The suggestion that there never was such a creature will be accepted by most authorities with something akin to relief The layman may even be tempted to say that the anthropologists have only themselves to blame In this branch of science the facts are scanty a tooth, a fragmented limb bone, a battered skull bone—meagre enough they are for the far reaching conclusions sometimes based upon them Yet it is only by the interpretation of such clues that we can expect the anthropological study of the ancestry of man to advance, and till now we would have been unreasonable to demand that anthropologists should always suspect every discovery of being an expert forgery

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1 *Lancet* 1953 i. 531
2 *East Anglian Times* Nov 12 1953
3 *Lancet* 1949 i 784

1 Weiner J S, Oakley K P, Le Gros Clark, W E *Bull Brit Mus (nat Hist)* 1953, 2 141

Special Articles

THE MOTHERS' AID (MØDREHJÆLPEN) INSTITUTIONS OF DENMARK

PREGNANCY: ABORTION ADOPTION

J D B Andrews
M.D Lond. D.P.H.
FORMERLY DANISH GOVERNMENT SCHOLAR STUDYING SOCIAL MEDICAL INSTITUTIONS

THE objects of the Danish Modrehjælpen (mothers' aid) institutions, as set out in the Act of 1939 are to provide for pregnant women and mothers with children, personal, social and legal assistance, advice and guidance during pregnancy and after confinement, and help with the support of the expected child. In addition, the Modrehjælpens are playing an increasing role both in the arrangement of adoptions and in giving general educational advice on motherhood, child care, and hygiene.

The seven Modrehjælpen institutions set up in 1939 are independent of each other but work in liaison. The Copenhagen institution, in particular offers advice to the others when asked. The cost is covered partly by the State and the county and borough councils, and partly by donations from private societies and individuals.

The councils of management consist of representatives of the State, local authorities, and private associations whose objects are in line with those of the Modrehjælpen. There is also a central Maternity Aid Joint Council which watches developments in the work of the various institutions and recommends to the Social Ministry such additional measures as may be necessary from time to time. All except one of the Modrehjælpen institutions have branches run by permanent staffs; thus many of the major towns in Denmark have their own full-time functioning Modrehjælpen.

The staff of the Modrehjælpen institutions consist essentially of

The head of the institution (generally a social worker or law graduate).

University graduates in law or sometimes economics.

Social workers who have had 2-3 years training at the Social School in Copenhagen.

Gynæcologists (one of whom often acts as physician to the Modrehjælpen).

Psychiatrists.

Clerical staff.

In their day-to-day work the Modrehjælpens give: social economic *and personal aid*; *legal aid*; advice on the possibility of obtaining a legal abortion and the special help available if permission for this is refused; family advice (in Copenhagen only); educational aid; and medical aid. They also arrange adoptions.

Social Economic and Personal Aid

The Modrehjælpen enables the mother to go through her pregnancy, confinement and early years of motherhood with a minimum amount of physical, social, and psychic stress to her and to her child. Cash gifts and loans are seldom given; the women receive the actual articles they are in need of, which helps them to realise that the social worker is taking a practical interest in their problems. Many towns have arranged for the distribution of free milk through the Modrehjælpen, and this makes it possible to keep in touch with most of the pregnant women in a particular area (about 87% in Copenhagen).

The doctor or midwife delivering an unmarried mother must inform the Modrehjælpen so that a social worker can visit her and find out if she is in any special need of help. In practice most unmarried mothers visit the Modrehjælpen of their own accord, before the child is born.

All unmarried pregnant women are entitled, after the birth, to free accommodation for themselves and their infants for a year if they want it. If there is no suitable home for them in the district, arrangements are often made for them to stay at a *private house—in many cases the home of a midwife.* The Modrehjælpen institutions also run homes for expectant mothers, as well as homes taking both expectant mothers and mothers with young children. They will also find mothers posts in private houses, where they can do domestic work both before and after their confinements, so remaining financially independent. Convalescent homes (mainly open in the summer) are maintained, where mothers with young children (generally under the age of 7) can stay for a week or a fortnight on production of a doctor's certificate saying it is necessary for their health. Again there are infant homes (for children under 2 years) which provide for infants waiting to be adopted or to be sent to foster homes found by the Modrehjælpen, as well as for infants whose mothers are unable to look after them temporarily but hope, in a year or so, to be in a position to do so.

Free milk is allowed to pregnant women (0·5 litre daily for 6 months before and 1 litre daily for 6 months after the birth). Where the home is very poor, Modrehjælpen sometimes adds to the furnishings or equipment. It also provides baby clothes for the child till it is 1 year old. Domestic help is arranged for the mother in her home both before and after the confinement; but this home-help service is mainly reserved for women who have unsuccessfully sought a legal abortion.

Legal Aid

PATERNITY

It is both the duty and the right of the mother of an illegitimate child to state who the father is; but even if the father admits paternity, the facts must be legally established. The Modrehjælpen gives the woman both legal and general advice on this subject.

There are about 2000 paternity cases at the Modrehjælpen in Copenhagen every year, and in at least half of these the father acknowledges paternity at once. In the remainder there is generally some obstacle or other to the establishment of paternity. In many cases the mother is both ignorant and frightened, and it helps her if one of the Modrehjælpen's legal assistants accompanies her to the law-court. In perhaps 150 cases yearly no clear decision is arrived at in the lower court. (In these cases, the father may have to contribute to the child's maintenance, but is not named the father.) Here the Modrehjælpen is sometimes able to find new evidence and fresh proceedings can be started. The court, in fact, often seeks the Modrehjælpen's assistance in solving difficult cases.

Once paternity has been established the illegitimate child has the same legal rights as if he were born in wedlock (in regard to such things as surname, inheritance). In addition, the father has to contribute towards the child's maintenance. If two or more men are putative fathers each of them has to pay the total amount, but the mother receives only one man's contribution. This sum is three-fifths of the cost of maintenance of a child boarded out as a foster child in a good home. The money payments are generally handed over to the local authorities and they in turn hand over the money to the mother. The Modrehjælpen often advances the money direct to the mother while the case is proceeding. This sometimes takes 3–4 months from start to finish. If a man accused of paternity wishes to have blood group tests carried out on himself and on the mother and child, the judge almost always agrees and accepts the specialist's opinion on the subject.

ABORTION

The legal personnel of the Modrehjælpen also give help in abortion cases of certain types.

Application can be made for a legal abortion on ethical grounds in a pregnancy which has resulted from an incestuous liaison. In such cases the law allows the paternity to remain unestablished. In a pregnancy resulting from a case of alleged violence or rape, or through excessive influence on the man's part, the woman must inform the police immediately after the incident if she wants legal abortion on ethical grounds to be considered In these cases the police work in coördination with the Mødrehjælpen Legal abortion is also permissible where a child under the age of 15 has conceived

If a girl under the age of 21 applies for a legal abortion, the legal guardian (usually a parent) must be informed. However, if the girl does not wish her parents to be informed she can apply for a trustee to act in the place of her guardian. In many cases a legally trained member of the Mødrehjælpen acts in this capacity

In Denmark a woman may have a legal abortion for one of the following reasons

A.—Medical Indications

(1) Where this is the only means of avoiding grave danger to her life or health (somatic or psychiatric)

(2) If the *medical* danger is not conditioned by sickness, but by social conditions (e g , exhaustion) a legal abortion can be granted under certain conditions (see below)

B.—Ethical Indication

When conception is the result of rape, violence, incest, &c , or conception has taken place under the age of 15

C.—Eugenic Indication

Where there is gave danger that because of hereditary predispositions the child will suffer from insanity, mental deficiency, other grave mental aberrations, epilepsy, or serious and incurable bodily disease

Before an abortion is considered by the Mødrehjælpen in category A(2) the woman is told by the Social Worker of the various ways in which her pregnancy, confinement, and period after the birth can be eased socially and economically, and she has to be informed of the danger to herself in having a legal abortion (as well, of course, as of having an illegal abortion) However, before it is decided whether a legal abortion will be advised on account of *any* of the above indications, the following procedure is carried out

In the case of a somatic medical indication being suggested, the woman is seen by a specialist in the particular field concerned if necessary, or is admitted to hospital for observation. In the case of a psychiatric indication the woman has a thorough psychiatric examination from one of the Mødrehjælpen's psychiatrists, and also, if necessary, is admitted to hospital for observation

In the case of an ethical indication the police have to be informed , and where rape is alleged the police interview and question the woman in detail Where the indication is eugenic the Institute for Human Genetics inquires into the personal and family history This institute has records of a very large proportion of the hereditarily tainted families in Denmark, including details of their admittance to hospitals or mental institutions, and the diagnoses made The institute sends a report to the Mødrehjælpen A " conditional " indication for abortion is said to be present when there are medical or ethical arguments in favour of a therapeutic abortion, and in addition there is a slight possibility of inheritance of disease Naturally it is generally impossible to give a percentage probability of a hereditary disease occurring in the offspring Legally, the case of a eugenic indication is treated separately from the question of sterilisation

In 1950, there were 702 applications to the Institute for Human Genetics for a legal abortion on genetical grounds , 626 of them came through the Mødrehjælpen, and 254 of these were granted, 279 were " conditionally " granted, and 93 were refused In addition there were 87 applications for legal abortion plus sterilisation, 71 coming from the Mødrehjælpen, of which 48 were granted, 21 granted " conditionally," and 2 refused

Procedure

The woman coming to the Mødrehjælpen seeking an abortion is generally referred there by her own doctor, but she can come direct if she likes Doctors are compelled by law to refer all women who come to them seeking abortion other than abortion for strictly medical [illegible] to a Mødrehjælpen

A social worker sees the woman, either at the Mødrehjælpen or in her own home, and takes a full social and medical history She confirms some of these details from the records of the child welfare committee, and the social offices, and often has an interview with the husband or other near relative. The case is then reported to the gynæcologist, who gives her a thorough general, obstetric, and gynæcological examination, and if necessary refers her to the psychiatrist A case-conference follows (in Copenhagen), and, if a legal abortion is thought necessary, the woman is referred to a surgical department of a hospital Before the operation is carried out two doctors have to give their consent , and in practice these are the surgeon undertaking the operation and the physician or psychiatrist attached to the Mødrehjælpen About a third of all women coming to the Mødrehjælpen (excluding those coming for free milk) are seeking legal abortions and, if the Mødrehjælpen decides that abortion is indicated, a full statement of reasons, with the case-history, is sent to the surgical department of the general hospital in which she will have the operation. Details of every case have also to be sent to the Medical Council after the operation has been done

Special Help

In 1948–49, 2321 women sought legal abortions in Copenhagen, and permission was given to 897, of whom 12 sought further help Of the 1424 refused permission, 265 sought further help from the Mødrehjælpen They are naturally entitled to all the usual help given by the Mødrehjælpen as well as the special help set aside for women who have been refused a legal abortion. This is specially designed to make their pregnancy, labour, and puerperium easier, and to provide better conditions for the child

In 1948–49 the Mødrehjælpen spent the equivalent of £1339 on furniture and equipment for the homes of patients, £435 in compensation for loss of work (mainly to unmarried mothers), £234 on other maternal expenses (clothing, rent, cash grants, and payments for the child in an infant home), £210 on mothers' debts and hire purchase instalments, £162 on home helps, and £161 on baby clothes and other equipment for the child (such as prams and cots)

The Mødrehjælpen also sometimes helps in training the mother in a trade (such as sewing), so that she may be able better to support herself and the child

Family Advice

About a third of the mothers seeking abortion give as their main motive family or personal conflicts In 1949 a family advice department was set up in association with the Copenhagen Mødrehjælpen, financed by the Social Ministry, where patients and their families could seek further social, psychiatric, and medical help

The staff consists of a psychiatrist, a psychologist, and three or four social workers They hold their sessions in the evenings so as to have a better chance of seeing several members of the family The social workers often interview the women in their own homes, and thus have a better opportunity to meet the father, who is sometimes unwilling to go out to a consultation But an effort is made in every case to see both wife and husband, as well as other members of the family concerned in the particular family problem (especially adolescent children, or the parents of the husband or wife) Patients are referred from a variety of sources—the school psychological services, psychiatric departments of hospitals (who send patients requiring aftercare), and general practitioners. In addition, some patients attend of their own accord. Many are referred from the Mødrehjælpen when permission has been refused for a legal abortion Results are often better where the patients have come directly from one or other of the Mødrehjælpen departments, as friendly relations have already been established. This also makes it possible to weed out apparently hopeless cases and so save the staff's valuable time

Most of the patients are married, some are engaged couples, or people living together, or single people with special sexual problems Most of them are in the younger age groups A very large number of patients relate their sent family problems directly to bad housing con ions. The main types of case seen by the family vice departments are

Women complaining of neglectful husbands, some of whom good husbands except for their addiction to alcohol
People seeking sexual education
Families in which one member at least has a neurosis or is ychopathic
Families whose external difficulties seem to be the main use of unhappiness (e.g the single mother with her child, ing in very poor conditions);
Sexual problems or unfaithfulness
Problems with adopted children.

Many of the patients need a combination of social, ychiatric, and medical help No deep psychotherapy is dertaken, but the patients are helped to adapt them lves better to their marriage partners and their rroundings. Group therapy is arranged once a fortnight der the direction of a psychologist and has helped eatly in giving patients social contacts A complete ck of friends and acquaintances has been very noticeable nong those seeking help from the family advice epartment.

Complete cures have been few but in well over half e cases the difficulties have been lightened and the milies have been better able to carry on In about a uarter the conditions remained the same but these atients were still being given help by the department ontact has been lost with most of the remainder except r a very few in which conditions worsened This evelopment, however was not unexpected in the cases question Separation or divorce was not as a rule dvised, though legal aid to these ends was given when t was sought.

Adoption

Adoption in Denmark is of two kinds

1 Where the parties to the adoption are acquainted and the mother of the child has access to the child (perhaps a quarter to half of all adoptions) In these cases, the adopting parents are often relatives of the mother

2. Where the adopters or the mother want a special clause inserted saying that the mother must not be allowed to see the child. In these cases the mother and the adopters are not acquainted (some half to three-quarters of all cases) In these cases the adoption must be handled by a body or person holding a special licence from the Ministry of Justice. The Modrehjælpen institutions, a few leading doctors, the heads of children's homes, and child welfare committees have hitherto held this licence but recently it has been decided that in future licences *will only be issued to* the Modrehjælpen institutions. At present probably about 80–90% of the adoptions with this clause in it have been arranged through the Modrehjælpen. In 1948–49 there was a total of 1052 adoptions.

A central department in Copenhagen now supervises all adoptions. This arrangement has given the Modrehjælpens wider choice of prospective adopters. The inter viewing of both the mother and the prospective adopters is done by the local Modrehjælpen As in other countries, there are more supposedly infertile couples wishing to adopt children than there are children free to be adopted so it is possible to choose the adopters carefully There are about three would be adopters for every child available, and many more wish to adopt girls than boys The waiting time at the moment is about 1–2 years The Modrehjælpen tries to place the children as soon as possible after they reach the minimum age (3 months) at which they can be legally adopted If the woman wants to have her child adopted, she does not as a rule breast-feed him or her unless the hospital where she is delivered makes breast-feeding a rule

The mother has the right to free accommodation for herself and her child at a mother-and-children's home for a year after the birth The Modrehjælpen makes sure as far as possible that the child is not being offered for adoption for financial reasons alone; if the mother needs help outside the scope of the Modrehjælpen she can get it from the child welfare committee Where adoption is decided on the social worker takes a full case history and asks about the father of the child—if possible interviewing the father as well. If there is any reason to think that there is some hereditary taint on either side, the Genetical Institute is consulted on the advisability of adoption

In 1950 out of 260 inquiries from the whole country the Genetical Institute reported that adoption was not contra-indicated in 162 cases, was indicated with reservations in 90 and was contra indicated in 6 In 2 cases no answer was made The Genetical Institute are often asked to say whether it is necessary to tell future adopters about the possibility of the child displaying some hereditary taint If the possibility is remote and will only worry the adopters, the Modrehjælpen usually favours silence

The social worker who sees the mother after the birth sees her again before the adoption takes place (at least 3 months later) to make sure she still wishes the adoption to take place

The physical condition of the child, and his mental growth and development is studied in a children's home. The mother can thus, if she wishes, take her child back without the prospective adopters being distressed—as they would be if the child was already living with them Where the advisability of adoption is doubtful it is often found wise to keep the child in the home for a year or more in order to assess its probable development.

The social worker at the Modrehjælpen, at her first interview with the adopters, asks them whether they have been to a doctor to have the cause of their supposed infertility investigated, and if they have not advises them to do so She then tells them of the legal and moral duties and rights of adopters.

Generally speaking the adoptive parents must be a married couple not under 25 years nor over 55 not suffering from any infectious disease and possessing some financial security They must have a certificate from the child welfare committee saying that they are considered suitable to adopt a child. The social worker asks whether the adopters have been in conflict with the law during the last 20 years; she receives information about their capital and income and interviews two people who have known the couple for many years she may also get a statement from a doctor or someone else who has known the couple intimately about the success or otherwise of their marriage their interest in children, and their motive for wishing to adopt. Lastly she visits their home and assesses its suitability

A conference on all the collected information about the child his or her parents and the prospective adopters, is held in the central department in Copenhagen The child's interests are regarded as absolutely paramount in deciding whether the adoption shall go through

Before adoption is completed the police interview both the mother and the adopting parents, and the case is then referred in most cases to the head of the county council If there are complications the papers are sent to the Ministry of Justice before being finally approved or rejected.

When choosing the parents, the Modrehjælpen takes various other factors into account thus, if the adoptive parents are living in a different locality from the mother she is less likely to see or hear of the child Then the Modrehjælpen tries as far as possible to place the child with people of similar intellectual capabilities and from the same milieu as its parents though naturally children coming from very poor homes are placed in better and more secure economic circumstances. Height, bodily habitus, and colour are taken into account so that there is some likelihood that tall people will adopt tall children &c

If the adoptive parents die or in the very rare cases where an attempt is made to annul an adoption order (for instance because the child proves to be oligophrenic) the legal advisers help to arrange a new adoption, or in the latter case advise the adoptive parents.

Medical Aid

The pregnant woman can be examined by a gynæcologist at the Mødrehjælpen, to confirm that she is pregnant, and she is also seen at least 3 times by the Mødrehjælpen doctor, and 3 times by the midwife during the pregnancy, and more often if necessary If she has any somatic disease likely to be adversely affected by pregnancy she is referred to a specialist and if necessary admitted to hospital Under the Pregnancy Hygiene Act, 1946, however, these duties now fall on general practitioners, as part of their service to members of the various health insurance societies

Educational Aid

Advice on health is given by the gynæcologist and the midwife when the woman first attends the Mødrehjælpen to have her pregnancy confirmed, and courses of lectures are arranged on various subjects such as hygiene of pregnancy, the proper nourishment of children, and child psychology. Classes in sewing and cutting are also held

General sexual education as well as instruction in methods of contraception, are undertaken by a woman gynæcologist

Research

Since 1947 a psychiatrist and 2 social workers have been following up 500 women who came to the Copenhagen Mødrehjælpen in 1943 seeking abortion The main aim of the research is to find out the long term results achieved by the three possible end-results

1. The woman proceeded to term (and either kept her child or had it adopted)
2. A legal abortion was advised
3. A "spontaneous" abortion took place (in many cases presumably due to illegal interference)

The practical difficulties of this social and psychiatric follow-up are great because the woman has often married, married again, or is living with parents who know little or nothing about the incident in question Much tact is needed

The Future

It is widely thought that the Mødrehjælpen should become a social institution used by the population as a whole, and not only by a particular section of it The free milk given to pregnant mothers is helping towards this goal as it is largely arranged through the Mødrehjælpen

Social and economic aid for women who have sought a legal abortion is provided from public funds, but the amount of private money available to help other pregnant women seeking help is very small indeed Flats are badly needed for single mothers with children (such as those provided in Sweden) where they can bring up their children in secure and homelike surroundings, one apartment house with 54 apartments has recently been opened in Copenhagen Educational establishments are needed where mothers (especially those who are single) can learn a skilled job, and so be able to support their child adequately More nursery schools would be welcome both for the children of mothers who have to go out to work, and for those of some mothers who are equally busy in the home Many think a law should be introduced forbidding employers to dismiss any woman on account of pregnancy (a law of this kind has been in force for a long time in factories) The loss of wages incurred by the women would be paid for out of public funds, so that employers would not have to bear the loss

The Mødrehjælpen institutions are only dealing with the fringe of the abortion problem More individual personal help and advice are obviously needed by women asking for an abortion Recent research carried out on women being admitted to two big hospitals in Copenhagen for the immediate after effects of an abortion showed that only 1–2% had previously applied to the Mødrehjælpen for a legal abortion A suggestion, successfully opposed in 1939, that there should be a social indication distinct from the medical indication for legal abortion is now being made again

Further development of the Mødrehjælpen institutions depends largely on whether sufficient public and private funds can be found to meet the growing scope of such an organisation, and whether interest in the institutions can be fostered among such people as doctors and lawyers, who are able to call public attention to the value of these centres and the need for their extension

Summary

The scope of the Mothers' Aid Institutions of Denmark is described They cover the whole of Denmark

The organisation gives medical, social, and legal help and advice to pregnant women and mothers with young children The daily work includes social, economic, and personal aid, legal aid, advice with regard to the possibility of obtaining a legal abortion, family advice, adoption arrangements, and educational aid

The institutions wish to become an agency for pregnant women and women with young children in general, and not only for those in social or economic distress. The social workers are the mainstay of the institutions, but in addition there are gynæcologists, psychologists, and lawyers attached to them

Probably the greatest advantage of the institutions is the comprehensiveness of the social aid they give. In other countries which have similar social welfare services the organisations concerned, both statutory and voluntary, are often widely dispersed

I would like to express special thanks to Fru Vera Skalts, head of the Copenhagen Mødrehjælpen, and Dr Henrik Hoffmeyer, psychiatrist attached to the institution, for the help they gave me while studying at the institutions in Denmark, and also to Fru Eva Knudsen for her help and kindness in the preparation of this article

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RECENT ADVANCES IN THE PROTEIN *FIELD*

THE nutrition panel of the Society of Chemical Industry held in London on *Oct* 28 the first of a series of meetings devoted to Nutritional Reappraisals. Mr A E BENDER, PH.D, discussed Proteins. He dealt particularly with two topics—the biosynthesis of the peptide bond, and protein nutrition

Our earlier views on the static nature of protein katabolism, defined nearly fifty years ago by Folin, were revolutionised by the work of Schoenheimer and Rittenberg using isotopically labelled amino acids. Whereas we used to believe that protein synthesis came to an end at maturity we now know that it continues even in the adult We picture a small but rapidly metabolising amino-acid pool, fed from the dietary proteins and in equilibrium with the structural and functional proteins of the body While single amino acids and incomplete mixtures can enter the pool and participate in the various equilibria, as indicated by the rapid entry of labelled amino acids into tissues, they cannot remain in the pool and they, or their equivalents, are immediately excreted

The amino acid pool is turning over at great speed; the half life period of human protein is 80 days, that of the liver and serum-proteins is 10 days, and that of the carcase 158 days Rittenberg has calculated that the pool consists of 0 5 g nitrogen per kg body weight, and that protein is synthesised at the rate of 1 3 g per kg per day, or 90 g for the average adult Such rapid and continuous breakdown and resynthesis of protein emphasises the question of how the peptide bond is synthesised One fundamental fact has been clearly established—that the synthesis of a dipeptide from two amino acids requires the intervention of the energy rich phosphate bond Many isolated tissues will take up labelled amino acids and the process can be inhibited by reagents which are known to stop phosphorylation After the synthesis of the dipeptide several possibilities exist. One is the stepwise addition of further amino acids under the influence of proteolytic enzymes, such as chymotrypsin, resulting in a lengthening of the peptide chain. A second method involves the transpeptidation reaction catalysed by cathepsin. In this process the first step is the synthesis of the two amides—glutamine and asparagine—and the tripeptide glutathione which requires a supply of energy These compounds then exchange a group with the peptide chain without any further expenditure of energy resulting in a lengthening of the peptide chain These methods have been shown to work in vitro, but we do not yet know whether they are the actual methods involved in vivo A quite different procedure has been postulated by Dounce who suggests that the nucleic acids act as templates governing the order of arrangement of amino-acids in the polypeptide chains. Dr Bender suggested that these findings hold great promise for the speedy answer to the problem of protein synthesis.

With regard to protein nutrition he said that recognition of the need to be able to express the nutritive value of the different proteins rather than to think of all proteins as being equal has been slow in spreading from the laboratory to the fields of practical application There are still many medical men who regard all proteins as one substance and do not appear to be aware of their differing nutritive values.

The biological measurement of the nutritive value of a protein is a long and relatively inaccurate procedure and a valuable contribution has been the demonstration that the percentage of the limiting essential amino acid present as compared with egg protein—i e the so called chemical score—is closely correlated with the biological value. This correlation appeared to hold despite the recent evidence that the amino-acid make-up of a protein is not the only factor involved. For example it has been shown that amino-acids may be present in a protein but not liberated during digestion and are therefore unavailable. This is of particular importance in the case of cooked and stored proteins where lysine combines with sugars and cannot be liberated by enzymatic attack. Another difference is in the site and rate of liberation of the constituent amino acids which also affect their availability

It has been shown that for protein synthesis all the essential amino-acids must be presented simultaneously to the cell synthesising mechanism: there is no storage For example, if five of the essential amino acids are fed at one meal and the remainder twelve hours later the animal dies of protein starvation Hence the rate of release of amino acids during digestion is a factor of some importance, and it has been shown that different proteins release their amino acids at different rates Thus it should be possible to have two proteins of identical chemical composition but differing considerably in nutritive value. Despite this, biological value has been shown to correlate with chemical composition

The immense practical value of being able to predict biological value from chemical composition has made re-examination of the position worth while. Analytical and biological data suggest that there is a different relation between the content of the limiting essential amino-acid in a protein and its biological value from that originally postulated by Mitchell and Block in 1946 A protein completely lacking one essential amino acid —i.e., with a chemical score of zero—has a biological value of zero A protein containing its full complement of amino-acids (that is having a chemical score of 100) is completely utilised thus having a biological value of 100 From this relationship Dr Bender suggested that each chemical score should correspond numerically with the biological value

That the revised chemical scores accord with this theoretical relationship only approximately is due to the low standard of accuracy at present attainable in amino acid estimations, as was demonstrated in the recent coöperative test organised by the Rutger's Bureau of Research. Better methods of amino-acid estimation together with further applications of the revised chemical score method, might lead to a wider use of actual nutritive value rather than the non specific description of proteins merely as proteins. Mr E M **Learmonth** discussed the abnormal proteins observed in the blood plasma of infants receiving deficient diets In the absence of the essential amino acid lysine plasma-proteins have appeared in which the lysine is replaced by non essential arginine. Such changes may be involved in the evolutionary processes.

Mr K J **Carpenter**, PH.D said that, despite the poor agreement between different laboratories in the Rutger's Bureau coöperative assay of amino acids in proteins, the results have been of considerable value and microbiological assay has provided useful information He asked whether biological value is an important factor in diets where a surplus of protein is consumed Dr **Bender** replied that, while it is not significant in Western diets, it is important where the diet contains minimal amounts of protein

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FELLOWSHIP FOR FREEDOM IN MEDICINE

Fear that a full time salaried health service is a real possibility was expressed at the annual general meeting of the Fellowship for Freedom in Medicine on Nov 21 at which Lord **Horder** presided The meeting reaffirmed the demand that private patients should be entitled to drugs under the same conditions as National Health Service patients, their doctors submitting to the same control in respect of prescribing as those in the service

Dr E C **Warner** (hon. secretary) reported that the medical and dental members of the Fellowship number 2530 compared with 3081 a year ago Those who left after the Danckwerts Award forgot that it was the Fellowship which had rescued arbitration from the wastepaper basket and insisted that it should again become the policy of the British Medical Association In the last few months there had been an increase in membership following the stand taken at the B M.A. Representative Meeting on the restoration of good will and the determination to resist a whole-time salaried service Speaking of the success of the Fellowship's pamphlet for doctors on the rights of the private patient under the N H S Dr Warner said that another leaflet was being prepared which could be handed to patients. Dr Warner emphasised that the Fellowship is not opposed to the B M A. as such. It had been able to make its voice effective in the councils of the association.

Dr G J V **Crosby** presenting the report of the general practitioner hospitals subcommittee, said that the general practitioner hospital is far more economical than the health centre General practitioners were being asked in some places to take on work from which they were excluded in 1948 and this again was a source of considerable economy

Dr J O M **Rees** secretary of the subcommittee on private practice called on the Fellowship to make drugs for private patients its target for the year

The meeting unanimously approved the programme of reform of the health service proposed by the Amending Acts subcommittee of the Fellowship This was presented by Dr A. C E **Breach** Asking that the possibility be examined of vesting the administration of the N H.S in an independent body composed of persons of national repute Dr Breach said that if medicine could once more be freed from politics there would be some hope The gradual, insidious onset of a salaried service was a real danger The greatest safeguard was the optional restoration of the right to buy and sell the good-will of general practices The subcommittee wanted to find ways of relating the remuneration of a doctor to the quality of his work, and not merely to the number of patients Other recommendations in the report were that there should be established under the presidency of someone of the standing of a High Court judge a permanent independent court of arbitration, that the method of constituting the local executive councils be adopted as a pattern for all other administrative committees, the relevant interests being directly represented, that regulations, orders, and "directives" should be issued only after consultations with appropriate interests, with arbitration in the event of non agreement, and that medical staff committees should be officially recognised Health centres should not be owned and controlled by local authorities and encouragement should be given to the formation of group practices by the provision of long-term, low interest loans In the interests of the public and the N H S itself, no opportunity should be lost of encouraging private practice The meeting agreed that the executive committee should act for the Fellowship when Dr Breach's subcommittee presented its further report on reform

A lay associates' committee was established, and to this was referred the question of drawing the attention of M P s to the provision of drugs for private patients

Lord HORDER, in his survey of the Fellowship's work, said that the Guillebaud Committee gave them a chance of saying once more that every time one shut out the general practitioner, one cost the patient and the country more time and money—and got less good results There was no economy without efficiency, as Disraeli remarked, and it was not efficient to eliminate the expert Lord Horder criticised B M A apathy in letting basic principles go downstream "they have ceased '*from mental fight*' We have not" It was not true that the public were in general thoroughly satisfied with the service Medicine must have freedom It must control its own career, it could not accept control from the State, least of all by party politicians He repeated what he had said ten years ago—if the nation wanted the best that medicine could give, this autonomy must be preserved against all comers

MYXOMATOSIS

THE PROTECTION OF LABORATORY RABBITS

IN response to inquiries the Laboratory Animals Bureau has issued some brief notes[1] on the steps which may be taken to protect laboratory rabbits against myxomatosis, a virus disease which has now spread from the Continent to parts of Kent and Sussex[2]

The bureau states that the infection is enzootic in certain wild South American rabbits, where it has a comparatively low mortality, but it is almost 100% fatal in European rabbits In the rare instances of natural recovery, permanent active immunity is established The disease has not been conclusively demonstrated in any other species

The virus is spread by bloodsucking insects, chiefly mosquitoes and midges, but fleas and other ectoparasites can carry it Infection may also occur by direct contact, and even human contact can convey the virus from an infected to a normal animal The incubation period is 4–5 days and death occurs from 3–10 days from the onset of symptoms The earliest symptom is blepharoconjunctivitis, followed by swelling round the nose and mouth, and a copious nasal discharge which is loaded with virus. Myxomatous swellings appear in various parts of the body, with rapid wasting and terminal pyrexia

Myxomatosis will readily spread to laboratory rabbits unless precautions are taken There is little chance of spread during the winter months, but it is very likely to flare up in the spring and summer Preparations for the protection of laboratory stocks should therefore be made without delay

(1) *Control of Vectors*—Wherever possible, vectors should be prevented from entering rabbit houses This will involve proofing windows, ventilators, and other openings against mosquitoes and midges, the provision of air lock doors, change of outer garments and footwear for those entering the rabbit house, and the use of insecticides within the house—for example, by means of aerosols To be effective, these precautions must be very thorough

(2) *Control of Cases and Contacts*—Immediate killing of cases in the early stage of blepharoconjunctivitis, burning the carcases, and disinfection of the cages, are essential precautions Contacts should be isolated for seven days Wholesale destruction of contacts, even of cage mates, is not necessary

(3) *Immunisation*—Vaccination with the Boerlarge strain of the Shope fibroma virus confers a strong immunity to myxomatosis lasting at least 12 months The vaccine is injected intradermally or subcutaneously, and immunity is established before the 14th day

If rabbits are obtained from another laboratory or from a breeder or dealer, the risk of their being infected must be accepted It would certainly be possible to arrange for the vaccination of accredited breeders' rabbits, and possibly of those of other breeders as well How far the bureau is able to help dealers will depend on the extent to which the dealers are willing to accept help and some measure of control.

An advisory committee on myxomatosis has been set up with Lord Carrington as chairman Until this has reported it is not possible to say where the vaccine is to be obtained, or what the recommended dose and vaccination technique are

GENERAL MEDICAL COUNCIL

OPENING the 187th session on Nov 24, Sir DAVID CAMPBELL, the president, paid a tribute to the work of the late Colonel Norman King, formerly registrar, who served the council from 1897 to 1933 As a new member he welcomed Mr Keith Paterson Brown, who now represents the Royal College of Surgeons of Edinburgh in place of Sir Henry Wade.

At its last session, Sir David said the council approved a method of election to the Medical Disciplinary Committee which while preserving the necessary degree of continuity in the membership will give each member of the council an opportunity to serve A similar scheme of election to the Penal Cases Committee will be proposed

Six years having passed since the publication of the current recommendations relating to the medical curriculum, the time is approaching when the council wil have to study the effects of these recommendations and consider how far it may be necessary to revise them in the light of the changing circumstances of medic practice In due course the council will be receiv reports from its visitors and inspectors, but meanwhil it will be asked to consider the desirability of hold a debate next May on the whole question of medi education, including the impact thereon of the co pulsory period of house-officer appointments

The council published last year a list of the hospitals Great Britain and Ireland and of the posts therein approv for the time being by licensing bodies for the purpose of hou officer service under the Act of 1950 That list included hospitals and 3048 posts Since then, the council has b informed that 53 other hospitals have been approved, wh 4 included in the list have ceased to be approved The numb of recognised posts has increased to 3232 A list setting o detail the changes both in the number of hospitals and posts as now been issued by the council for the guidance of all ncerned.

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[1] Supplementary Memorandum to L.A.B News Letter no 7 (January 1954) Copies may be had from the bureau, at the Medical Research Council Laboratories, Holly Hill, London, N W 3

[2] See *Lancet*, Nov 14, 1953 p 1031

Licensing bodies are empowered to approve for this purpose ospitals not only in this country but also in the Common ealth and in foreign countries, and the council has now sued a list showing the hospitals and institutions in Colonial rritories which have been formally approved by one or ore licensing bodies for an indefinite period The list also ets out the posts which have been recognised in each hospital. he council understands that a number of licensing bodies hile not necessarily dissenting from the revised and con olidated list of hospitals and posts recommended earlier n the year by the Colonial Office intend to consider on its erits each case in which one of their graduates wishes to e employed in hospitals in Colonial territories.

After speaking with regret of the approaching retirement of Mr Frederick Winterbotham as solicitor to the council the President concluded by referring to cases in which there have been fraudulent dealings by general practitioners under the National Health Service In one case a practitioner obtained money from the local executive council by submitting forms relating to the treatment of temporary residents whom he had not in fact treated In another case a practitioner had been convicted in a court of law of fraudulently charging fees to patients who were on his N H S list.

"The Penal and the Disciplinary Committee have reason to believe that the cases in which inquiries have already been held are not the only cases in which a practitioner has wrongfully obtained sums of money from the executive council or has improperly demanded and accepted fees from patients on his National Health Service list I desire therefore to take this opportunity of bringing to the notice of the whole profession the gravity of offences of this nature A conviction in such a case inevitably brings an offender within the disciplinary jurisdiction of the council; and in instances where no conviction has occurred it is nevertheless open to the Penal Cases Committee of the council to refer to the Disciplinary Committee for inquiry any case duly reported to them in which there appears to be a prima facie case that a practitioner has been guilty of such serious unprofessional conduct

Public Health

County of London Census Figures

The full 1951 census figures for the County of London have now been published.[1] Details for other counties in England and Wales will appear at short intervals. The total population in the area of the County of London at the 1951 census was 3 347 982, representing a net decline over the whole period since the 1931 census of over a million, most of which has occurred since 1939 The dwellings in the county, occupied by private households or vacant, now number 820 918 Since the last census in 1931 some 100 000 new permanent dwellings have been erected, nearly one-third of them since the late war Some 70,000 dwellings were totally destroyed by bombing during the war; and 30,000 new dwellings have been added since the war as a result of conversions. There has been a further reduction in the over-all density of occupation of dwellings from 0 98 persons per room in 1931 to 0 83 persons per room in 1951—largely due to the increase in the proportion of small households. The proportion of persons aged 16 and over in full time education in London was more than twice as high in 1951 as in 1921, when the question was last included in the census. Comparison of the figures for the County of London and for England and Wales suggests that, both in the younger and the older sections of the occupied population the duration of full time education has been slightly longer in London than in the country generally no doubt owing to the migration to the Metropolis of disproportionately large numbers in the higher administrative and professional occupations.

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[1] Census 1951: County Report London. H.M Stationery Office. 12s 6d

Symposium

PHENYLBUTAZONE

EMPIRE RHEUMATISM COUNCIL'S DISCUSSION

In the two years which have elapsed since the first report[1] from this country on the treatment of rheumatic diseases with phenylbutazone, a considerable fund of experience of the effects of this important drug has accumulated Its actions and dangers have been the subject of considerable controversy, and in choosing phenylbutazone as the subject of the first of a series of symposia the Empire Rheumatism Council provided a useful opportunity for an interim stocktaking As the chairman of the clinical section, Dr W S C **Copeman**, pointed out the intention of the meeting on Nov 13 was to provide objective data rather than current views and experience

Relief of Symptoms

The ability of phenylbutazone to produce subjective relief in a high proportion of cases of rheumatoid arthritis was amply confirmed. Dr O **Steinbrocker** who described his extensive observations in the U S.A had found a significant analgesic effect in about 70% of his cases and improvement in function in about 50% with very definite benefit in 23% Dr G R **Newns** (Sheffield) had compared the effects in early and advanced cases; symptoms were relieved in 70% in each group and the good response of advanced cases was confirmed by Dr F **Dudley Hart** (London) Dr J H **Jacobs** (London) had found that failure to respond tended to occur in those clinically active cases with a high erythrocyte sedimentation rate.

While there is no serious disagreement about the proportion of cases obtaining subjective relief views on the extent of objective changes are less uniform. The figures quoted at the symposium were in general agreement with earlier reports on subjective responses during the early stages of treatment and it was perhaps of more interest to hear how patients had fared during long-continued courses. In Dr Newns's series of 197 cases 65% were still taking the drug after six months; 13% had dropped out because of failure to respond ab initio 7% because the initial response had not been maintained, and 14% because of toxic effects. In a rather longer follow up of 17 cases Dr Steinbrocker had seen 8 instances of relapse or interruption of improvement by toxic complications. Dr J P **Currie** (Glasgow) reported that 82 out of 131 cases maintained on treatment for a year or more were still improving while none had failed to enjoy continued relief of symptoms. It appears, therefore that while an immediate favourable response cannot always be maintained, either because of relapse or of intolerance a useful proportion of patients can benefit from prolonged treatment

In ankylosing spondylitis Dr Steinbrocker had found a good analgesic effect from phenylbutazone Dr G D **Kersley** (Bath) commended its use in cases which had failed to respond to radiotherapy, and Dr Dudley Hart had found the drug particularly valuable in advanced cases.

Antirheumatic Action?

The important question whether or not phenylbutazone has a specific antirheumatic action was discussed by several speakers. It is not easy to lay down criteria which must be satisfied before any therapeutic agent can be credited with such an action A drug capable of exerting an anti inflammatory eff which is general, or even confined to inflammation a particular type, cannot strictly be held to be anti rheumatic, even though it may suppress all or some of the manifestations of rheumatic inflammation But a stronger case can be made out for a drug which profoundly influences the pain of rheumatic diseases, yet is not definitely effective in non rheumatic pain, and which suppresses the local and systemic signs of inflammation in these conditions The situation would be clearer if the inflammatory phenomena of diseases as clinically heterogeneous as rheumatic fever, rheumatoid arthritis, and gout could be accepted as sharing a common pathogenesis

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[1] Currie, J P 2nd European Rheumatology Congress Communications, p 417

Prof R **DOMENJOZ** (Saarbrucken) provided evidence that phenylbutazone has a suppressive action in several types of experimentally induced inflammation in animals —though Prof G A H **BUTTLE** (London) had been less successful in demonstrating this—as well as its analgesic, antipyretic, and anti-histamine effects The anti inflammatory action was retained in adrenalectomised animals, and phenylbutazone caused no depletion of adrenal ascorbic acid in hypophysectomised animals, showing that it exerted no pituitary corticotrophin-like effect

Dr Currie pointed out that the effectiveness of phenylbutazone and of other drugs in rheumatic diseases paralleled their ability to inhibit the development of œdema after the injection of irritants in animals The anti-histamine, analgesic, and antipyretic activities of the drugs compared (antipyrin, amidopyrine, isopropyl antipyrine, and phenylbutazone) were much less closely related to their therapeutic potency in rheumatic diseases He also emphasised the low analgesic potency of phenylbutazone in normal humans and in animals, as well as in pain of non rheumatic origin—cephalgia, migraine, trigeminal neuralgia, and root pain in intervertebral disc lesions Similar poor results have been reported [2] elsewhere in intervertebral disc disease, nerve root pressure, and migraine, though good analgesic effects have been claimed in postmenopausal osteoporosis[3] Paget's disease,[4] and "neuritis and radiculitis"[5]

Variable results have been obtained in osteo arthritis [2-4] Dr J S **LAWRENCE** (Manchester) found aspirin rather better than phenylbutazone in this condition and in non articular rheumatism Dr **FRANCIS BACH** (London) had been specially impressed by the results in osteoarthritis of the hip, and Dr **PARSONS**, speaking as a general practitioner and a patient, was enthusiastic about his results, particularly in old people

Dr Currie believed that good evidence of a specific antirheumatic action was afforded by the prompt response to phenylbutazone of the fever and arthralgia of rheumatic fever, now well established,[3 4 7-9] and of the symptoms of acute gout [3 10-12]

In rheumatoid arthritis, evidence of an anti inflammatory effect is generally sought in changes in the size of swollen joints and in the erythrocyte sedimentation rate Dr Steinbrocker was dubious about any true antirheumatic activity, though he mentioned some early good results from the injection of phenylbutazone into joints Dr R I **MEANOCK** (London) and his colleagues and Dr Dudley Hart were not convinced that joint swelling was affected by the treatment, though Currie et al.[13] have claimed a definite reduction, particularly in early and acute cases, and they have suggested that divergent views on this point may arise from the varying proportion of such cases included in individual series. The majority of those at the symposium thought that the erythrocyte sedimentation rate was not influenced by phenylbutazone, though Dr Lawrence believed that a reduction sometimes occurred, and he pointed out that a concentration in the blood of 10 mg per 100 ml could retard sedimentation in vitro

C reactive protein, which rapidly disappears from the blood during the treatment of rheumatoid arthritis with cortisone or corticotrophin,[14] was not affected in 2 of 3 cases investigated by Dr A G S **HILL** and Dr M **SAXTY GOOD**, but in the 3rd a weak reaction disappeared, possibly as a result of spontaneous improvement

The present situation seems to be that an antirheumatic effect is hard to define and that the action of phenylbutazone in this regard has not been convincingly established. Certainly there is no suggestion that the drug has any curative action—relapses after stopping treatment follow as promptly and as regularly as they do after cortisone

Increase in Coagulation-time

A hitherto unrecognised effect of phenylbutazone was described by Dr J G. **HUMBLE** (London), who found that a small proportion of patients receiving the drug had a prolonged coagulation-time The investigation was prompted by Hart's observation of a fall in capillary resistance in some of his patients An isolated instance of a prolonged clotting-time has also been reported.[15] Dr Humble's inquiries led him to the conclusion that the phenomenon was due to a true deficiency of prothrombin, it could be reversed by giving vitamin K, or by stopping phenylbutazone The development of this coagulation defect was related to the daily dosage level, rather than to the duration of treatment. Dr. Humble declined to speculate on the obviously important possibility of a relation between this effect and the occasional occurrence of gastro intestinal bleeding during phenylbutazone treatment

Some Metabolic Effects

Dr R M **MASON** (London) helped to clear up the confusion which has existed about the effect of phenylbutazone on uric acid metabolism The urinary excretion of uric acid in individual cases depends on the balance between water retaining and mild uricosuric actions. In general, increased elimination of uric acid was sufficient to explain the well established lowering of plasma-uric-acid concentration This uricosuric effect, leading to urate precipitation in the urinary tract, was suspected to be the cause of oliguric death in a case of gout treated with phenylbutazone [16]

The effect of phenylbutazone on the excretion of water and electrolytes was discussed by Dr P O **WILLIAMS** (London), who considered that sodium was retained by reason of a specific increase in tubular reabsorption and that water retention was a secondary effect The output of potassium was unaltered In most individuals, the effect was not progressive and ceased after 1 to 3 litres of water had been retained Œdema was not to be expected unless already present in subclinical amounts, but in patients with diminished cardiac reserve the increased water load may precipitate failure Diuresis occurred after treatment was stopped, and occasionally, as Dr Kersley pointed out during continued treatment Similar observations have been reported by American workers.[17] Dr Domenjoz referred to the retarding effect of phenylbutazone on the elimination of *p* amino salicylic acid, morphine, and penicillin—presumably due again to an action on renal tubular function

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[2] Kuzell W C Schaffarzick, R W , Brown, B , Mankle, E A *J Amer med Ass* 1952 149, 729

[3] Kuzell W C Schaffarzick, R W *Bull rheum Dis* 1952 3 23

[4] Davies H R. Barter R W , Gee, A , Hirson C *Brit med J* 1952 ii 1302

[5] Kling D H American Rheumatism Association, 1952 See *Ann rheum Dis* 1952 11 299

[6] Steinbrocker O Berkowitz S Ehrlich M Elkind M Carp S *J Amer med. Ass* 1952 150 1087

[7] Bunim J J American Rheumatism Association 1952 See *Ann rheum Dis* 1952, 11 299

[8] Feldman, H A. *Ibid*

[9] Fleming J Will G *Ann rheum Dis* 1953 12 95

[10] Kidd, F G Boyce K. C Freyberg R. H *Ibid* p 20

[11] Mason R M *Ibid* p 82

[12] Stephens, C A L jun , Yeoman F E Holbrook W P Hill D F *J Amer med Ass.* 1952, 150 1084

[13] Currie J P Peebles Brown R. A , Will G *Ann rheum Dis* 1953 12 88

[14] Hill A. G S *Lancet*, 1951, ii, 807

[15] Cudkowicz L , Jacobs, J H. *Ibid* 1953 i, 223

[16] Bowers V H *Brit med J* 1953 i, 617

No comment was made on the interesting effect of phenylbutazone on iodine metabolism During the early stages of treatment the uptake of iodine by the thyroid is depressed, apparently as a result of competition by the drug, which has an affinity for iodine; when this affinity is satisfied thyroid uptake reverts to normal [18 19]

Blood Concentration

A relation between the concentration of phenylbutazone in the blood and the therapeutic and toxic effects was described by Dr Meanock and his colleagues A daily dose of 1200 mg (high by present standards) produced a peak level in the blood after about ten days and elimination might not be complete till fourteen days after stopping treatment. A blood level of 5 to 10 mg per 100 ml produced the maximum subjective response and any increase served only to aggravate the danger of toxic effects. Control of dosage by measurements of the concentration of the drug in the blood cannot become generally feasible, but the results suggested that a suitable schedule might be an initial dose of 200 mg per day increased, if necessary, by steps of 100 mg to a maximum of 500 or 600 mg daily

Toxicity

We have lately discussed [20] the hazards of treatment, and they were considered in detail at the symposium Prof E C DODDS, F.R.S who took the chair at the experimental section, pointed out that the part of the molecule of phenylbutazone responsible for its toxicity was unidentified. There was perhaps a possibility that a related compound of equal therapeutic potency but reduced toxicity may eventually be produced.

Dr Steinbrocker had encountered toxic effects notably nausea weight gain, and rashes, in 22% of the cases in his large short-term series although there were no serious incidents among these patients, he considered that the use of the drug was fraught with hazards and that the general attitude in this country was over-optimistic Dr Newns reported a rather similar incidence of toxic effects, including another fatal case of agranulocytosis,[21] bringing the total now reported to 6 [22–25] Those examples of agranulocytosis, and others which have not proved fatal,[3 22 26–31] have all developed within the first six weeks of treatment Dr Steinbrocker insisted as have many others, on the necessity for weekly white-cell counts, but those who believe that this does little more than induce a sense of false security were supported by Dr Kersley who described an instructive case [26] in which vomiting diarrhœa, rash, and fever gave warning of impending trouble, while the white cells of the peripheral blood showed no abnormality The administration of phenylbutazone was stopped at once, but agranulocytosis did not appear until four days later Several speakers thought it essential to warn the patient to stop treatment at once and to report if fever, malaise, or sore throat developed. Dr Meanock had seen one death—an elderly patient in whom oliguria may have been precipitated by phenylbutazone.

Previous reports have thrown suspicion on phenylbutazone as the probable cause of fatal gastro intestinal bleeding [32] perforation of duodenal ulcers,[22] sudden unexplained death [6] and aplastic anæmia.[33] Jaundice has occasionally been seen during treatment, but it is hard to be certain that the drug was responsible and both Dr Domenjoz and Dr Buttle had found no histological evidence of a hepatotoxic effect in animals Ulceration of mucous membranes may occur in the absence of agranulocytosis, and Dr Steinbrocker referred to a varicose ulcer which tended to heal when phenylbutazone was withdrawn and to break down when it was given again

Dr Currie seeking to explain the discrepancy between the comparative insignificance of toxic effects (none of which had given him any anxiety) in his own very large series and the more sombre experience of others, wondered whether the simultaneous administration of barbiturates, which he was careful to avoid, might increase the dangers Certainly in several untoward incidents phenylbutazone was not the only drug being given, and Dr Steinbrocker had seen an alarmingly high incidence of gastric bleeding when it was given at the same time as gold. In our correspondence columns this week Dr Belart discusses some possible causes for the apparent discrepancies in the published reports about toxicity He favours Butapyrin' (phenylbutazone and amidopyrine) as less toxic than phenylbutazone and he finds that toxic effects are reduced if this preparation is given intramuscularly and in short courses using relatively large doses

Although the incidence of toxic reactions of all kinds in most of the published series has been high (30 to 50% in the majority) most have been mild and have not necessarily stopped further treatment. In avoiding toxic effects it may be important to appreciate three facts phenylbutazone persists in the body for a long time after a single dose failure to achieve an adequate response to a daily dose of 600 mg is an indication for abandoning treatment rather than for increasing the dose (unless, as occasionally happens the tablets are not being absorbed) and the intake should be reduced as rapidly as possible to the minimal effective level Careful selection of patients may also help though it is unfortunate that the drug may be particularly dangerous in elderly patients in whom the analgesic effects may be so valuable Certainly it is wise to exclude individuals with poor cardiac or renal function. Gaps in treatment of any ten to twenty days may increase the danger of sensitisation [26] but Dr Steinbrocker believed that a break in treatment of a few days every two weeks might be good policy

No single method of treatment is appropriate for all patients in all stages of rheumatoid arthritis and phenylbutazone is no exception—nor unfortunately is it alone in carrying a measure of danger The realistic clinician ' *as Dr Steinbrocker named him reviewing what has been* tried and what resources are left to him may find it difficult, on occasion to deny a patient badly in need of help a drug which may give him ease His decision may become simpler when further careful observations have defined the extent of the risk he has to accept, and no doubt the Empire Rheumatism Council will return to the subject of phenylbutazone at a future symposium

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[17] Wilkinson E. L. Brown, H. *Amer J med. Sci* 1953 225 153
[18] Scott, K. G., Frerichs, J B Reilly W A. *Proc. Soc exp Biol., N Y* 1953 82 156
[19] Green, T W, White, W E Engleman E P Krupp M. A. *Ibid* p 155
[20] *Lancet*, 1953 i, 1226
[21] Newns, G H. *Brit. med J* 1953 i, 992
[22] Procter J D., Evans R. G *Lancet* 1953 i 1047
[23] Dilling, N V *Ibid* p 1230
[24] Steinberg C LeR. Bohrod, M. G Roodenburg A. L *J Amer med. Ass.* 1953, 152 33
[25] See *Brit. med. J* 1952 ii, 1427
[26] Kersley G D., Mandel L. *Lancet* 1953 i, 1010
[27] Charet, R., Siegel, I *J Amer med. Ass.* 1953 151 556.
[28] Bernhot, E. Oxman, A. C. *Ibid* p 557
[29] Werblow S. C., Neber J *Ibid* p 1280
[30] Ehly J M., Stickney J M *Proc. Mayo Clin* 1953 28 241
[31] Lateman, L. P American Rheumatism Association, 1952 See *Ann. rheum. Dis.* 1952 11 207

[32] Benstead, J G *Brit med. J* 1953 i 711
[33] Leonard, J C. *Ibid* p 1311

The Widdicombe File

IV (2) —ALL IN THE DAY'S WORK *

MY DEAR BREWER,

I am glad to know that you intend to do some of your own clinical pathology We all have a weakness for that mythical beast, the old horse and-buggy doctor, who, between daily tracheotomies and nightly cæsarean sections, cured every hysteric for miles around by force of personality alone You will be his lineal successor Do not be afraid of poaching my preserves The proper province of the general practitioner is everything which he can do without interfering with all his other duties If your venture does no more than spare me and my colleagues some wasted hours looking at normal fluids and excretions we shall be in your debt

May I make some brief comments on your plans ? The M R C hæmoglobinometer is a lovely yoke I just wonder if for your job it is not rather like using a Purdy gun for scaring blackbirds The main fault with almost every method of measuring hæmoglobin is that you must do so with a pipette Now cleaning pipettes is a nice healthy job, but it must be done while the blood is wet If you are called away as you are about to do it you will either have to put in a lot of work with caustic fluids or buy a new pipette (And you would be surprised how many blocked-up pipettes there are in the backs of the cupboards of the most conscientious doctors) There used to be a hæmoglobinometer—there may be still—which did not require a pipette but measured the blood by allowing a thin film to run by capillary action between two glass plates a fixed distance apart When you had finished you merely wiped the two glass plates clean with some dry gauze or your handkerchief There is too another trick which I learned from one of the elder brethren while sitting on a medical board Apparatus required needle, 1, corner of white blotting paper, 1 piece Prick the patient and take a small drop of blood on the paper Prick yourself and put your drop beside it Compare If your blood contains 14 5 g of hæmoglobin per 100 ml (or more or less) you will be able to detect a comparative pallor in his or her specimen if it contains 10 g or less *Probatum est* as the old books on magic say

Why use Leishman's stain ? Jenner's is easier to make and to use and leaves you in no doubt whether a cell is a lymphocyte or a large mononuclear Incidentally I used to prefer it on æsthetic grounds. I am sure you are right to eschew the counting of blood cells But if you own a hæmocytometer keep it handy Rarely, very very rarely, there are times in the middle of the night when a knowledge of the total white cell count is worth a lot Any fool can do sedimentation-rates to interpret them demands mental powers of a very high order Before you stain your vaginal swabs look at them wet —i e, in saline First you will see that some of them, despite the volume of the discharge, contain almost no pus at all but masses of desquamated epithelium Pass them by I do not know the cause or cure of this condition but I never find any infective agent in these smears Trichomonas is plain to see but I would take no heed of monilia (candida in the best circles nowadays) unless accompanied by pus Lastly I am all in favour of your syringe service It will cost a lot but it seems to come nearer to perfection than most of the tricks used by your colleagues. When the practice can run to it, buy a small electric dry steriliser I have known women so ignorant that they thought meringues more important in the domestic oven than glassware

A sprinkling of clinical pathology can bring much éclat and quite a lot of new patients to a practice. I have seen it happen When your practice has expanded to the point when the laboratory bench is used to house record cards——I will not go on May I add two words more ? Fascinating though all the gadgets are when they first arrive I believe that the mere performance of these tests will pall in time Set yourself a plan which will keep your mind as well as your fingers busy How many men and women are doing their daily job with less than 12 g of hæmoglobin per 100 ml ?, We know a lot about hospital admissions and expectant mothers but not much about the ambulant population How many young men show positive tests for occult blood who have neither ulcers nor piles ? My other precept is a graver one Never believe your results if they contradict your other observations or common sense " I beseech you, in the bowels of Christ, think it possible that you may be mistaken " Noll had the right idea An unshakeable certainty of the correctness of his own findings is the surest hallmark of an inferior clinical pathologist

Yours sincerely,

HARRY HAWKE.

N.B —Always prick the lobe of the ear and not the finger, they can't wriggle so much

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*Dr Hawke is here answering Dr William Brewer's letter published on Nov 14

Medicine and the Law

Hospital Charged with Inadequate Supervision

SHORTAGE of staff in a small hospital proved to be no defence in a recent action at Monmouthshire assizes [1]

A patient who was admitted to hospital at 2 P M, was suffering from pneumonia The sister on duty stated that he had shown no sign of being irrational when she handed over charge to another sister at 8 P M According to the counsel appearing for the patient's widow, the delirium stage of pneumonia had been reached There were signs by 8 20 that the patient was slightly irrational and by 11 30 that he was definitely in that condition Some time between 1 30 A M and 3 15 he left the ward in his pyjamas with a blanket round his shoulders He tried to enter the cab of a lorry which had stopped temporarily at traffic lights The driver, being forbidden to give lifts to passengers, refused him entry Eventually the body was recovered from the river Wye, some strips of the blanket being found on each side of a bridge At 3 25 of the night on which he disappeared he was reported to the police as missing as from 3 15 It appeared that an entry " patient walked out between hours of 2 A M and 3 A M " had been pasted over the original entry "*fairly comfortable night* "

It was contended for the defence that the patient might have got up and walked out if he had remained at home The judge did not regard this argument as excusing the hospital He held that the night sister and the orderly on duty with her were negligent in leaving the man unwatched There was also negligence in the staffing of the hospital The defendants knew that the patient was suffering from a dangerous disease and that delirium at some stage was likely A medical witness, called by the plaintiff, had expressed the view that one trained nurse and a ward orderly with a night porter were insufficient night staff in relation to the case The hospital matron said the system of locking the outside doors of the hospital and leaving the key on the inside was the best possible

Damages of £3049 were awarded by the judge to the widow and infant daughter

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[1] *Western Daily Press*, Nov 11, 1953, *South Wales Echo*, Nov.

Parliament

Fog and Public Health

In the House of Lords on Nov 18, Lord **Amulree** rew attention to the danger caused by fog to the health f the people of London and asked what progress had been made in making available an adequate supply of smokeless fuel for domestic use It was estimated that, during he fog of 1952 4000–5000 people died from the effects of he fog, and the sickness claims for the Counties of London and Middlesex were doubled Recording machines howed that during the fog the concentration of sulphur dioxide in the air was five times the normal of the previous hree days. Great care was taken about the purity of food and water, but not so much about the air which Lord Amulree pointed out, was one of the most important foods we took in Smokeless fuels would go far towards abolishing fog, and a second remedy was the formation of smokeless zones by local authorities under the Public Health Act 1936 He wished to know what treatment was given to the fumes from the large power stations All these remedies, he admitted, would cost money but fog was also expensive in its effects on public health

Lord **Haden-Guest** believed that one of the difficulties in London at any rate was the absence of any central authority dealing with London as a whole He thought we would have to forbid altogether in the London area the use of fuel which emitted smoke

The **Earl of Selkirk**, Paymaster-General replying to the debate, said that there was little danger to health from pure fog the danger only arose from polluted fog He went on to compare the 1952 fog with the cholera epidemic of 1866 when the Thames was an open sewer and 14 000 people died Enormous sums of money had been spent on public sanitation since 1866, and the cleansing of the atmosphere would demand much the same resources. Smog was no danger to people in good health, but people with heart or chest diseases should seek their doctor's advice. A mask would give some protection against solid particles, but he agreed that it would not protect the wearer against the gaseous contents of smog

Turning to the smokeless fuels, he said that they cost about half as much again as coke. Unless their cost was brought within reach of the average householder he doubted if they would make more than a small though valuable contribution to smoke abatement. The total quantity on the market was less than 1 million tons, against 85 million tons of coal and 3 million tons of coke But progress had been made in changing over to smokeless fuels. London for instance was consuming no more coal, but more smokeless fuel, than it was ten years ago, while the domestic consumption of gas had gone up by 50% and of electricity by 100%. The public, he added should be warned against banking up fires at night in foggy weather In London it would not be enough to create small smokeless areas as had been done in Manchester and Coventry unless similar action were taken to windward in neighbouring districts.

Capital Expenditure on Hospitals

On Nov 16 Mr **Cyril W Black** asked the Ministry of Health to reconsider their refusal to sanction small structural alterations at the Nelson Hospital, Merton The proposed alterations, which had been approved both by the group management committee and by the regional hospital board, would cost about £3000; and need only about 1¼ tons of steel and about 0·5 standards of timber The regional hospital board was unable to provide the money, but King Edward's Hospital Fund had offered to provide the sum necessary Yet the Ministry of Health had refused to sanction the project owing to the Treasury arrangement for capital allocations

Miss **Patricia Hornsby-Smith** parliamentary secretary to the Ministry said that the Minister would greatly regret if there were any suggestion that he did not welcome help from voluntary sources for the health services But it must be understood that for capital projects they still had to conform with the overriding national policy The present system of controlling capital investment was based on economic considerations which extended beyond the control on Government expenditure as such, and even beyond the control on building materials. As a result the allocation of the Ministry of Health must cover all hospital work, however financed, and if a regional hospital board accepted money from outside it still had to toll against their own over-all capital allocation.

Private Members' Bills

Colonel **Malcolm Stoddart-Scott** who was successful in the ballot for private members Bills, on Nov 18 introduced a measure to make it compulsory for the exchange of certificates of medical examination between persons before marriage. The second reading has been fixed for March 20

On Nov 18 Mr **G D N Nabarro** presented a Bill to amend the law as to the fees and allowances payable by coroners to witnesses to persons summoned to attend as witnesses, and to medical practitioners making post-mortem examinations at the coroner's request The second reading has been fixed for Feb 12

QUESTION TIME

Examination of Limbless Pensioners

Replying to a question Mr **Osbert Peake**, Minister of Pensions and National Insurance said he had not yet received the final report of the Rock Carling Committee on limbless pensioners. The special examination of several thousand pensioners for which the committee had asked was taking longer than expected.

Mr **C J Simmons** Cannot the Minister give us any idea at all when this committee will report? They have been sitting for an inordinately long time and these limbless pensioners are dying at the rate of 1000 a year I am very angry about this and I hope that the Minister will realise that the men for whom I am speaking need immediate attention and not procrastination Mr **Peake**: The committee was composed almost entirely of doctors and they disagreed among themselves. As a result we are undertaking this considerable examination of some 4500 limbless ex-Service men. We want it to be a thorough examination because the results of the inquiry will be of world wide importance. I regret that the examinations are taking longer than was at first expected. I hope they will be completed early in the year but after that the results will have to be brought together and examined

Replying to a question Brigadier **J G Smyth**, parliamentary secretary to the Ministry of Pensions and National Insurance, said that the number of deaths among limbless pensioners during the five years ended March 31 1953, were 674, 717 758 and 874 respectively

Capital Allocations for Mental health Services

Mr **H A Marquand** asked the Minister of Health for which years since 1950 circulars were sent to regional hospital boards advising them to set aside for expenditure upon mental health services, a minimum proportion of their capital allocations what those percentages were for each year and what was the total capital allocation to the hospital service in each of those years.—Mr **Iain Macleod** replied: Annual circulars from 1950 onwards about hospital capital programmes have stressed the need to make appropriate provision for mental health but none of them has mentioned a specific percentage The following figures show total capital allocations to the hospital service annually since 1950 and the proportionate value of mental health projects included in the programmes of regional and teaching hospital boards or financed outside their programmes:

	Total capital allocations £ million	*Proportionate value of mental health projects*
1950–51	9·5	15%
1951–52	9·0	21%
1952–53	7·9	18%
1953–54	8·0	15%
1954–55	10·0	

* Hospital board programmes not yet available but 13·5% of allocation set aside centrally for mental health projects. This is in addition to the provision that will be made by hospital boards.

Dentists Bill

Mr **Frank Beswick** asked the Minister if in view of the delay in proceeding with the Dentists Bill, he would bring forward that non-controversial part which would make it possible for dentists with qualifications obtained outside the United Kingdom to practise in this country —Mr **Macleod** replied No. The Bill will be reintroduced in full when Parliamentary time permits.

In England Now

A Running Commentary by Peripatetic Correspondents

MANY people have noted the decline of that fine old medical institution, the Bedside Manner, but no-one has recorded the rapid and significant rise of its usurper, the Bed-end Manner Yet this new technique of commenting on patients' lesions, treatment, and prognosis from the foot of the bed rather than from the side is one of the really big developments in Medicine in the past couple of decades The phrase is a complete comment on the gradual abandonment of physical signs and the substitution for them of the broad-spectrum (if I may use a popular word) investigation

It is in hospitals that the Bed-end Manner flourishes, and I have seen some of its finest examples in the teaching hospitals The first important principle is that no doctor shall approach a patient alone all approaches must be made en masse during the Grand Round This effectively prevents any single doctor from speaking confidential and comforting, if highly unscientific, words to the patient This means in effect that nobody ever speaks to the recumbent victim except an occasional wardmaid and the man with the newspapers No doctor must utter a sound, since it is obviously "someone else's duty to undertake that type of thing" The en-masse approach also prevents a salutation at any level between physician and patient, because as the caravan approaches the bed the Chief stage-whispers "What is she ?", the menial turns to answer the question, and the golden moment is gone

History-taking, a transient and ever-dwindling procedure, may still be undertaken by a house-officer in the lamentable absence of a dictaphone or a suitable "cross out that which does not apply" type of questionnaire But happily many other scientific devices for keeping the doctor from the patient have been perfected Auscultation is unnecessary in view of the electrophonograph, the electrocardiograph gives us the pulse-rate, and the lowered serum-potassium tells us that it is full The barium meal shows us the cause of his vomiting, and the ventriculograms give a cause, if not the original one, for his headaches "His cardiac catheterisation leaves us in some doubt, Sir" "Yes, yes, ahem, you'd better repeat it" Pulse charts and temperature charts are consulted only if the patient is seriously ill and the diagnosis obscure, and much of the value of the latter is lost by the enthusiasm of the house-officer, who achieves uniformity of temperature throughout the ward by giving massive doses of the latest 'mycin to every patient By these means all moves to the bedside are obviated, unless to remove a bedpan or on some similar mission—duties that are carried out at an appropriate level

Above and beyond all, the patient must be told nothing If he is in a surgical ward and has keen hearing, he may catch the word "Thursday," which means that he will have his operation on Thursday If he is in a medical ward, he may hear the explanatory remark "catechol amines" which means that he will have his cate . (whatever they are) estimated

The Bed-end Manner is a sign of changed medical times all right Still one can't help feeling—just now and then of course—that this change means more to the patient than antibiotics, anæsthetics, electrolytes, psychiatrists, old uncle Tom Cobbleigh and all Graph-paper has replaced the leech in therapy Is either ideal ?

* * *

Having occasion to travel to the Outer Isles at a time when all good sailors are reading the trade journals for home berths my friend found himself at his destination dealing with the combined ravages of post mal-de-mer and active mal-de-terre Only the hope of dying, he affirms, kept him alive on the voyage

However, not for nothing does my friend treat peptic ulcers with bottles and soul-searching talks With this spirit of medical faith and determination he hurried aboard on the evening of his homeward voyage filled to his pharmacological capacity with three brands of anti-seasickness pill, scorning in passing their official equivalent, plus a double dose of the barbiturate he usually reserves for old ladies with high blood pressure and no housework Shakily he made his way to his lower berth in the depths of the ship

He states that on the whole he had a good night. True he found himself on the floor twice Once he was certain that they had turned turtle and he would have abandoned ship, but his fingers were inextricably enmeshed in the rack where his clothes should have been Nevertheless he was inclined, all in all, to be satisfied with the triumph of medicine over the elements

It was only when he arrived on deck next morning that he felt unwell "Och, yes indeed," said the captain sympathetically "Wass it not the wild night, last night It is a terrible pity we were not able to leave the pier at all, at all" It was now Sunday, my friend had no more pills, and the chemist was an elder in the kirk

* * *

I have just thought of a way of getting a lot of money for psychiatric research We point out to the Government that the atomic bomb and its offspring are being outmoded and that the next war but one will be fought with psychological weapons They will then earmark a couple of million for us, for Defence Prototype E.E.G. machines will be dashed off at enormous expense and at super-priority Vast tracts of the country will be taken over to discover which holiday areas are the most satisfactory for rehabilitation Beautiful country houses will be allotted to the training of registrars. B O A.C planes will be full of consultants hopping from London to Paris, then over to Washington We shall have steel and bricks for the asking, and can build hospitals The Russians will claim to have invented psycho-analysis. Senator McCarthy will state that unconscious motivation is an un-American activity Hollywood will make a film about the life of Freud, with six new hit tunes.

* * *

My peripatetic colleague who complains that so many letters in the correspondence column being "I have read with interest" does not seem to realise that letters reaching the Editor do not always leave his office unmodified Thus a letter written in heat to the Editor might read

"If your correspondent had the nous to turn the nut on the CO_2 cylinder to the right he might find his anæsthetic mortality reduced"

On emerging from the editorial mill of good manners this might well read

"I have read with great interest Dr Smith's letter on his increasing parabola in anæsthetic mortality These are difficult days and gas is not what it used to be Moreover, the machine itself is manifestly manufactured to confound and confuse It is constructed on very similar lines to modern poetry, almost impossible to comprehend, but one feels that beneath it all is a meaning and use However, Dr Smith may find it an advantage to turn the nut on the CO_2 cylinder This is done by turning the spanner clockwise"

* * *

The Mad Electrolyte's Lament

Oh, if only I had a slide rule,
In my tiny little head,
I could please the white haired doctor
And get back to my own wee bed

But our union rules are rigid,
We must spurn the grammes of men
And the dance that we dance together
Pays no heed to the decimal ten

I've tried a reducing diet
To get my weight down to my pal's
But all that has happened is fission—
So look out for schizoid squalls !

I've asked the membrane potential
To let me out once again
But he says now he doesn't know me
So I'm still in my little pen

Oh, doctor, please forgive me,
If I can't be as clever as you.
I don't understand your units,
But I do know what to do

Letters to the Editor

SUBCLINICAL POLIOMYELITIS INFECTIONS

SIR,—Your leading article of Nov 14 might be read as the last word in the discussion on the Prevention of Poliomyelitis which engaged your columns recently If so, I am at issue with you on several points.

(1) Few students of poliomyelitis would agree that sufficient facts have been marshalled to justify your conclusions. You say "Quarantine restrictions against poliomyelitis have been likened to closing the stable door after the horse has bolted They are better compared to mending the bottle after most of its noxious contents have already escaped, the attempt to prevent the last few drops from escaping however desirable, should be viewed in the light of the damage already done This new evidence [Melnick and Ledinko [1]] will discourage the adoption of stricter quarantine measures.'

(2) Dr Melnick is an eminent microbiologist He is well aware of the complexities of the serology of virus diseases [2] and might feel uncomfortable as your main support when you lean towards inaction You have not mentioned his evidence [1] that at Winston Salem the upper socio-economic group appeared to escape infection during the 1948 epidemic This suggests that, even at the end of an uncontrolled epidemic, there was a 'limited selective distribution' [3]

(3) In 1950 I said [4]:

> "During 1949 two or more cases in a household were not infrequently reported. This seemed to happen when there was a particularly high incidence in a hamlet village or small town. Already this year there have been several instances; for example in the Isle of Wight there were three cases of disease in each of three households The phenomenon is interesting because when it occurs a chain of contacts between households can be defined more easily than is usual in poliomyelitis and the disease appears to be spreading in a narrow stream of the population, healthy intermediaries or persons with ill defined illnesses providing some of the links.

And in 1952 [5]:

> Some of my colleagues and myself have come strongly to the opinion that poliomyelitis virus causing *disease* moves through a narrow stream of the population.

It is important to distinguish between 'disease' (now printed in italics) and 'infection' in the serological sense * Melnick [1] also comments upon certain similarities in the distribution of persons with poliomyelitis antibodies and with antistreptolysin. In regard to scarlet fever we do not base control measures upon antistreptolysin titres but upon manifestations of the disease.

(4) Examples of 'narrow stream' spread have now been recorded by many field workers. The phenomenon is capable of description and as such it has the qualities of a fact which cannot be ignored. Moreover, it is a phenomenon which until recently had not been seriously considered in framing our concept regarding the epidemiology of poliomyelitis It seems very probable that disease-producing polio virus is far from ubiquitous,[3] and that there may indeed be hope of devising general measures for controlling its spread.

(5) There may be some uncertainty regarding the word 'quarantine,' which means detention or limitation of the freedom of movement of persons who may transmit disease—a method nowadays rarely used in the control of any disease smallpox included. It is simple enough to stop typhoid carriers infecting others without quarantine when they understand the problem While I agree with you that stricter quarantine measures are not indicated in the control of poliomyelitis, I believe there is new evidence which encourages greater effort to prevent the case and the contacts from spreading infection, particularly at the beginning of an outbreak The matter is discussed more fully in the *Medical Officer* of Nov 21 and a more authoritative statement by a W H O expert committee is to be expected in the New Year Your readers will I think wish to suspend judgment.

Wimbledon. W H BRADLEY

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[1] Melnick, J L, Ledinko, N *Amer J Hyg* 1953 58 207
[2] Melnick, J L. Papers and Discussions of 2nd International Conference on Poliomyelitis. London, 1952 p. 301
[3] Francis, T *Trans. Ass. Amer Physns.* 1952 65 176
[4] Bradley W H. *Mon. Bull. Minist Hlth Lab. Serv* 1950 9 203.
[5] Bradley W H. Papers and Discussions of 2nd International Conference on Poliomyelitis. London 1952 p 366.
* [illegible]holm properly quotes me as saying elsewhere "study of the spread of the disease through some communities has made us consider the probability that the infection moves through a relatively narrow stream of the population."

THE INSULIN MYTH

SIR—Dr Bourne's article (Nov 7) should not go unchallenged because I feel that some patients would undergo much unnecessary suffering if his views were generally accepted. I wonder how much insulin treatment Dr Bourne has himself given before putting them forward. Having used both insulin and E.C.T in the treatment of schizophrenia since 1937 I have still not the slightest doubt of the clinical superiority of insulin in many patients, though the best results can sometimes be obtained when both are skilfully combined.

Dr Bourne's selected statistics remain unconvincing when one knows the number of other statistical studies and opinions he has glossed over or omitted including those of Mayer Gross a recognised world authority on schizophrenia and its treatment, Freudenberg, Müller Finiefs and Polonio He also omitted to point out that opinions on this matter were collected from many countries for the International Congress of Psychiatry in Paris in 1950 and then analysed by Neveu [1] who found *that insulin was the generally accepted treatment for* this condition. Insulin is certainly not a specific treatment for schizophrenia but the best we have available at present for many patients in the early stages.

Finally is there anybody in this country who has had several years, continued personal experience of *both* insulin and E.C T in this condition in large numbers of patients, and who really believes E.C T to be the better routine treatment of the early case? If so I do hope they will write and say so

Department of Psychological Medicine
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London S E 1 WILLIAM SARGANT

SIR—One must congratulate Dr Bourne on putting forward his views so forcibly supported by selected quotations His commentary on the use of insulin in schizophrenia demonstrates how easily irrational therapies are introduced how readily they are accepted, and how hard they die

1953 may be a convenient time to review the position because insulin therapy for schizophrenia was introduced just twenty years ago Since then a great deal of time, money, effort, journal space, and hope have been devoted to this particular biochemical method of directly attacking the psychotic's brain Bellak [2] lists over 700 references in the period 1936 to 1946 alone.

The particular 'difficulties of assessing any treatments in schizophrenia' to which Dr Bourne draws attention are of course seen throughout the field of psychiatric therapy For this there are three main reasons. Firstly 'the lack of mental theory in psychiatry' [3] leads to wide variations in diagnosis from psychiatrist to psychiatrist and from hospital to hospital. Secondly psychiatry is peculiar in that the criteria of improvement are vague, ill defined, and highly subjective, both from the patient's and the therapist's point of view Psychiatry is in fact uniquely backward among the medical sciences in that signs and symptoms are equated with the disease itself —because the nature of the disease process is so little understood This lack of distinction leads to treatments aimed at abolition of symptoms, and the acceptance of recession of symptoms as the measure of improvement Yet it is open to question whether, for instance, a schizophrenic temporarily deprived of the overt signs and symptoms of his illness—a state of what might be called induced anosognosia—is more normal or even better off in the long run The third difficulty in assessing therapeutic results is that physical methods by which psychoses are at present largely treated are entirely empirical What anatomical, physiological, or other basis there may be for their action is still a matter for speculation and hypothesis—a fact recognised by their most ardent advocates Further, physical methods of treatment themselves produce an abnormal picture, characterised by loss of spontaneity, loss of memory for recent events, diminution or loss of overt signs and symptoms of illness, and increased socialisation and hence easier management These are taken as evidence of therapeutic success, and little attention is paid to the price in concomitant over-all reduction of mental function During and after recovery from such treatments, the signs and symptoms of the underlying illness may remain permanently in abeyance , or they may recur—an eventuality which Dr Bourne graces with the description " relapse after withdrawal (of) convulsion therapy " Whether in such circumstances repeated administration of physical treatments with the recognised risk of permanent brain damage is justified, will remain doubtful till we have the results of long-term studies If this question is to be decided on assumptions—and Dr Bourne's statements on convulsion therapy are of this nature—one might assume with equal justification that the need for maintenance doses arises from, and is an indication of, failure of the initial treatment

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[1] Neveu, P International Congress of Psychiatry Reports. Paris 1950 vol. 4 p 77
[2] Bellak, L. Dementia Præcox. New York. 1948.
[3] Macalpine I Critical Evaluation of Psychosomatic Medicine *in* Modern Trends in Dermatology edited by R. M. B MacKenna. London, 1953.

I therefore take strong exception to Dr Bourne's statement that " the schizophrenic patient may be as dependent on E C T for a normal existence as a diabetic is on insulin " Such a comparison is surely as much an affront to the scientific physician and the physiologist as it is a grave danger to the schizophrenic Unlike the use of insulin in diabetes, shock treatments are empirical and unbiological, and neither their mode of action nor their effect is measurable The argument that shock treatments cause no mental impairment, as judged by psychological testing, does not carry much weight even after leucotomy, in which areas of cortex are destroyed, isolated, or removed, psychological tests are often reported as not revealing organic deficit The only possible conclusion is that the tests themselves are of limited value

Guy's Hospital,
London S E 1

RICHARD A HUNTER

SIR,—Dr Bourne's article contains a number of assertions and claims which cannot be allowed to pass without comment

The article, in effect, is a special plea for E C T in preference to insulin coma therapy in the treatment of schizophrenia He attempts to support his case by reference to selected papers and to results obtained in a group of soldiers suffering from schizophrenia

A number of important papers on the value of insulin are not mentioned—e g , Mayer Gross,[1] Bond and Rivers,[2] Bond and Shurley,[3] Garmany,[4] and Finiefs [5] The work of Freudenberg [6] is not given the attention it deserves

Dr Bourne discusses possible fallacies in attempts to evaluate treatment methods for schizophrenia, but gives no evidence to indicate that he has dealt with these in his own series His group is highly selected, as it consists of soldiers No details are given on methods used in assessing recovery His follow-up refers to only half the group and he relies on information obtained by letter for his follow up assessment It is doubtful if any reliance can be placed on information obtained in this way There is no evidence to show that the groups treated by different methods are in fact comparable in important respects Finally he ignores the time factor in assessment, the importance of which I have stressed,[7] and to which Dr Russell Davies refers in his letter (Nov 14)

It is very doubtful if any valid conclusions can be drawn from Dr Bourne's data Comparison of schizophrenia groups treated by different methods will be vitiated unless it can be shown that the groups correspond not only in age and sex distribution, but in clinical status and tendency to spontaneous recovery All groups should be assessed by the same standards and criteria and preferably by the same person

Dr Bourne makes reference to a number of isolated points in an article of mine [8] He pays little attention to the methods used to deal with the inherent pitfalls in attempts at assessing psychiatric treatment methods, but stresses what appears to him to be a numerical discrepancy which I am happy to explain He refers to a group of 18 patients who failed to respond to various methods of treatment He incorrectly assumes that all 18 patients received E C T , insulin, and electronarcosis The actual position was that all 18 patients received insulin and E C T , and of these 9 had electronarcosis as well This amplification of the data explains the apparent discrepancy

To deal with further points raised by Dr Bourne, I am able to say that the group of 160 schizophrenics studied were not derived from a larger group, but were consecutive admissions over a period He assumes that the E C T dosage was inadequate In fact the majority of patients treated by E C T had 25–35 treatments and some as many as 50 In a paper [8] to the International Congress of Psychiatry, statistically controlled studies showed that insulin-coma therapy was the only method giving significantly better results than routine hospital care The results gave no support to Dr Bourne's claim of the superiority of E C T in the treatment of schizophrenia Furthermore the relapse-rate with insulin was much lower than with E C T or electronarcosis In no patient did E C T produce recovery after insulin had failed, whereas in 16 patients in whom intensive E.C.T produced no improvement, insulin coma therapy resulted in recovery or considerable improvement

Dr Bourne points out that any positive results obtained in chronic patients may be regarded as significant In a group of patients with long standing schizophrenia of poor prognosis, insulin was the only method giving total recovery, which was achieved in 8·4% of such patients treated with insulin and in none treated by E C T or electronarcosis.[9]

The complexity of psychiatric material and the inherent difficulties of assessing psychiatric methods of treatment demand the rigorous application of scientific, statistical methods with adequate controls and follow up studies over long periods Dr Bourne will have to provide data which meet scientific requirements before his claim for the superiority of E C T over insulin-coma therapy in schizophrenia can be accepted

Cardiff.

LINFORD REES

SIR,—Many will sympathise with Dr Harold Bourne's youthful impatience and his critique of the empiricism of modern physical treatments in psychiatry , but very

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1 Mayer-Gross W *J ment Sci.* 1947 93 25
2 Bond, E D Rivers T D *Amer J Psychiat* 1944 101 62
3 Bond E D , Shurley J T *Ibid* 1946 103 338
4 Garmany G *J ment Sci* 1946 92 801
5 Finiefs L A *Ibid* 1948 94 575
6 Freudenberg R K *Ibid* 1947 93 9
7 Rees, L Recent Progress in Psychiatry London, 1953, vol II p 635
8 Rees, L International Congress of Psychiatry Reports Paris 1950 , vol. 7 p 4
9 Rees L *J ment Sci* 1949, 95, 625

w will agree with him when he replaces what he calls e "insulin myth" by a plea for convulsive therapy, eoretical dissatisfaction equally refers to either rocedure. As to insulin-coma therapy, against which is attack is directed—i.e., Sakel's method of treating hizophrenics by hypoglycæmia—this has been severely nd authoritatively criticised for many years—for stance by Bleuler,[1] who based his objection on statistical aterial of his own observation Nevertheless most linicians have refused to abandon the method and others ave even resumed it during the last few years. The easons are explained in Max Müller's monograph which ou recently reviewed[2]: it is the only treatment that olds out some hope of shortening and relieving schizohrenia, the major medical and social problem which r Bourne wants to save from the "mere parochial oncern of psychiatrists", he does not say to whom he ants to hand over the treatment of these patients My wn views on the treatment are still those I expressed in 947[3] and 1950[4] when I compared results obtained at richton Royal with an untreated control material from he Maudsley Hospital chosen for their *optimal prognosis* n 1938.[5] Both groups had been diagnosed by the same linician according to the same diagnostic determinants. If I may be allowed to quote one result of my ollow-up study of 454 schizophrenics treated between 1939 and 1947, I found that after three years 57% were total or social recoveries as against 34.5% of the control group It was also shown that although insulin therapy does not prevent relapse, it does not provoke it, after shortening the attack of the illness. Relapses can be successfully treated by another course of hypoglycæmia a second and third time—in what proportion will be the subject of an investigation of our follow-up office in 1954. That hypoglycæmia—like the treatments for cancer and tuberculosis—has its best results in early cases, and that it helps patients with a tendency to remission, can only speak in its favour because it supports Nature's curative tendencies. That it has to be combined with general rehabilitation to yield its full effect, seems equally natural to the clinician who looks at his patient without theoretical blinkers Moreover the rationale of hypoglycæmia as a therapeutic procedure is thanks to the work of Quastel, Himwich and Gellhorn much better founded than one would deduce from Dr Bourne's article I must not encroach further on your space by repeating what I have said before on the non-specific nature of the treatment, on the rôle of the insulin fit, on the combination of coma with convulsions, and on the other worries of our critic How plausible it would have been to write a paper on the 'salicylate myth' before and even immediately after the discoveries of the antirheumatic effect of cortisone and A.C.T.H !

Department of Clinical Research
Crichton Royal, Dumfries.　W MAYER GROSS

MILLI EQUIVALENTS

SIR,—In his letter of Nov 7 Dr Ennis draws attention to the difficulties facing clinicians in their interpretation of results expressed as milli-equivalents in acid base studies. I sympathise with the viewpoint expressed, for I have found no subject in medical and scientific work over 20 years, more difficult to grasp than that of acid-base balance. I feel that perhaps the subject is made obscure and muddling by unnecessarily loose and careless terminology It should be possible to explain mechanisms of pH variation without reference to the words acid, base, acidosis, alkalosis &c, with more exact emphasis on the essential nature of the change —i e that of hydrogen ion concentration

Electrolytes are now so fashionable that I feel that physiologists and pathologists should make every effort to clarify the subject. A start could be made in medical schools new literature, and new editions of textbooks, so that we may begin to have a generation of doctors who feel no antipathy to biochemistry and have no difficulty in the use of the term '*milli-equivalents.*'

Kingston Hospital Surrey　P DAGNALL.

TOXICITY OF PHENYLBUTAZONE

SIR,—I should like to draw the attention of your readers to the fact that on the Continent phenylbutazone was first tested pharmacologically and used clinically in 1949[1-3]

It was chiefly employed as 'Butapyrin' ('Irgapyrin'), consisting of phenylbutazone and amidopyrine (750 mg of each injected intramuscularly in 5 ml.) In spite of the fact that this drug has been extensively used, it has proved to have a very low toxicity But it is striking how often toxic effects occur in Anglo-Saxon countries, where pure phenylbutazone is employed Is this apparent discrepancy in toxicity due perhaps to greater reticence on the part of Continental doctors in publishing their failures, or is toxicity on the Continent in actual fact less ?

From my own experience over a period of five years in about 1000 cases treated with butapyrin and an equal number treated with phenylbutazone I think I can say that untoward reactions are much less frequent here. What is the explanation ? I think there are three factors : the first concerns the drugs themselves and the second and third the mode of administration.

(1) I, too found phenylbutazone more toxic than butapyrin Whereas with butapyrin, apart from œdema and rashes I met with no side-effects of any consequence (and certainly no case of agranulocytosis) untoward effects with phenylbutazone were more frequent, although much less so than in English and American reports. Besides œdema, I saw 1 case of severe gastric hæmorrhage 3 of massive hæmaturia, 2 of purpura, and 4 of severe angioneurotic œdema. This striking difference between the two drugs is surprising, for one would expect butapyrin to be more toxic in view of the large amount of amidopyrine it contains. One wonders whether the two substances have antagonistic actions, making butapyrin less toxic. I found support for this thesis in a case of massive hæmaturia in a 31 year-old man, who had had for eight days 800 mg of phenylbutazone daily The hæmorrhage recurred after the administration of phenylbutazone was resumed. But later there was no hæmaturia, when he had 1200 mg of butapyrin daily

(2) In England and America phenylbutazone was introduced in dragée form. This led to smaller doses being given (600 mg and less per day) but treatment was continued for weeks and months. On the Continent butapyrin came on the market only in high-dose ampoules (750 mg of phenylbutazone) The technique was developed of giving butapyrin in short courses of 3–5 high-dose injections at intervals of one or two days. This boost therapy proved particularly *valuable in acute and subacute attacks of rheumatoid arthritis,* degenerative joint diseases, and fibrositis. But here the drug is not used for prolonged treatment of rheumatoid arthritis. This Continental method of administration may perhaps be one of the reasons for the rarer occurrence of untoward effects since it is clear that when the drug is given for short periods sensitivity phenomena are less frequent.

(3) A further reason for thinking that injection technique reduces toxicity is provided by Brodie and Burns.[4] They showed that phenylbutazone in man combines very firmly and quickly with protein. When it is given by mouth this change takes place in the blood ; when it is injected intramuscularly however the change occurs in the muscle protein Therefore the serum level of the drug rises much more rapidly when it is given by mouth. The "shock effect of the dragées is thus greater This is perhaps the reason why of my 10

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[1] Bleuler M. *Z ges. Neurol Psychiat.* 1941 173 553.
[2] Müller, M. Die körperlichen Behandlungsverfahren in der Psychiatrie. Vol. I Die Insulinbehandlung Stuttgart, 1952.
[3] Mayer-Gross W *J ment Sci.* 1947 93, 25
[4] Mayer-Gross, W *Ibid* 1951 97 132.
[5] Guttmann, E., Mayer-Gross W Slater E. T O *J Neurol Psychiat.* 1939 2 25

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[1] Wilhelmi, G *Schweiz. med. Wschr* 1949 79 577
[2] Belart, W *Ibid* p 58[illegible]
[3] Gsell, O Müller W *Ibid*, 1950 80 310
[4] Brodie B. B. Burns, J J *Congr int. Rheum.* 1953

toxic cases, 5 had been treated with dragées—a method which I personally rarely use

For these reasons, it seems to me advisable to choose intramuscular injection rather than the oral route, short courses rather than long ones, and butapyrin rather than phenylbutazone

Zürich **WALTER BELART**

URINARY EXCRETION OF CITRATE

SIR,—Our preliminary communication of Sept 26, reporting very low rates of excretion of citrate in the urine during potassium deficiencies, was made because we thought the observation interesting, although we were unable to explain it On the basis of some findings of his own, Dr M D Milne (Oct 3) suggested that the fall in citrate excretion in our experiments could be explained by a diminished urinary excretion of calcium Indeed, according to Dr Milne, there might have been a greater fall in citrate than we observed Our analyses, however, which have now been completed, show that the urinary excretion of calcium was not reduced during our experiments, indeed the output of calcium in the urine was sometimes greater during the potassium deficiency than it was during the control periods, although we used a cationic exchange resin to produce the potassium deficiency This is in keeping with the finding[1] that, although the resin may combine preferentially with calcium in vitro, it did not increase the fæcal excretion of calcium in experiments similar to those in which the observations on citrate were made

It would seem, therefore, that our results cannot be explained along the lines suggested by Dr Milne and that there must be some other reason for the fall in citrate excretion

Medical Research Council,
Department of Experimental Medicine,
Cambridge

PAUL FOURMAN
J R ROBINSON

THE DRUG BILL

SIR,—I suggest that one of the best ways of keeping the N H S drug bill under control would be to cultivate a healthy sense of therapeutic nihilism That literally millions are spent each year on medicines is testimony to our pathetic credulity as doctors It is often stated that doctors are much under the influence of the manufacturing chemists, but the doctor who allows himself to be unduly influenced by the manufacturing chemist's blurb must surely be very young or very naïve, or both, and in this, and in many other things, it is only Time; presumably, that will bring a cure Or does the elderly doctor sometimes fall as easy a victim, on the principle that there's no fool like an old fool ?

During the late war, rendered almost desperate by the importunity of some old lady demanding something I didn't quite know what, I gave her—let it be confessed—a prescription for Mist Ferri Aperiens, without any regard to her particular complaint The next week her gratitude was almost maudlin in its excess because, as she said, my medicine had given her " such a lovely sleep " Equally surprising are the patients who tell you that they have a " wonderful appetite " as a result of taking a bottle of Mist Sod Salicyl Perhaps it does have that effect on some people Who knows ? But it wasn't what I was taught to expect

A recent copy of *Prescriber's Notes* gives details of the surplus drugs recovered from a patient's house following his death The total cost of these was stated to be about £40 Those of us who rarely write a prescription without at least bestowing a little thought on its cost and the probable extent to which it will really help our patient, can only sit back and meditate (without undue smugness) upon the mentality of doctors who squander the nation's resources with this kind of reckless prodigality

G P

ISCHÆMIC NECROSIS OF THE STOMACH

SIR,—I think the unfortunate complication of a subtotal gastrectomy, described by Mr Rutter (Nov 14), can be attributed not so much to devascularisation as to a possible technical fault in planning

His description of the first operation, where he removed the whole of the lesser curve, is rather confusing, since at the second operation he found an ulcer on the lesser curve, but it would appear that the necrotic ulceration was due to the nature of the operation—i e, Bilroth I—whereby extreme tension is placed on a partially devascularised cardia

I would suggest that had he closed the duodenum and constructed a Roux's en Y gastrojejunostomy, either retrocolic or antecolic, preferably retrocolic, the complication he described would probably have been avoided

Memorial Hospital, Peterborough **D W BRACEY**

LACTIC ACID IN THE TREATMENT OF OSTEO-ARTHRITIS

SIR,—Dr Lawrence, in his article of Oct 31, ended his summary " It is concluded that lactic acid has no therapeutic action in osteo arthritis " In fact, surely, his paper justified no such conclusion The most he was entitled to say was that the addition of injections of lactic acid, for a short period, to adequate physiotherapy make no difference in cases of osteo arthritis To warrant the conclusion which Dr Lawrence drew, he must compare untreated cases with cases treated only with injections of lactic acid, and I venture to think he might have reason to change his opinion

It was in a thoroughly sceptical frame of mind that, following a visit to Mr Grant Waugh's clinic at Darlington, I started injecting procaine lactic acid in some of my more obstinate cases of osteo arthritis six years ago The first cases had all received physiotherapy for a long time, and the average duration of symptoms was over four years Because of my scepticism these patients received no psychological boost from me to aid their improvement, but their degree of betterment was such that very soon this clinic " snowballed," so that for the last five years an average of 100 injections of joints have been given weekly, in spite of the fact that we only inject as a routine once a fortnight Being rather overwhelmed by these numbers, we often try to cut down the attendances by dismissing, for three or four months, all cases whom we do not find we are benefiting objectively The majority of these return to ask for more injections because, although they do not improve with them, they do get worse without them I would suggest that in cases of osteo arthritis of long duration, eight weeks is much too short a period in which to assess results, especially in hip joints, which I agree respond poorly to this form of treatment

It is probable that Dr Lawrence and I view this matter from very different standpoints He is a consultant dealing with " male employees of the National Coal Board "—in other words, with patients who, while off work, can rest as much as he requires them to and who, working or not, can attend hospital as often [illegible] necessary for treatment As one of the fast dwindling group of practitioner specialists, I see the patients in their daily lives as well as at hospital—women and the aged, as well as men of working age, and people who have to be transported to hospital from a radius of [illegible] miles Moreover, owing to economic difficulties, the physiotherapy department is extremely overcrowded and understaffed, so there are several other factors to be considered

In practice one fights a continual battle of compromise between what is the best possible treatment for a patient and what is the best treatment possible for that particular patient A major factor is the time spent not only by the patients but by those attending them—in this case doctors, transport drivers, physiotherapists, and those at home who do the work of the patients while they are attending hospital.

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[1] Fourman, P *Brit med. J* 1953, I 544

From my own experience I would suggest that in very many cases one injection of procaine lactic acid, given every two to four weeks, combined with simple home exercises, keeps a patient as mobile and pain free as two or three attendances a week at the physiotherapy department Neither is a cure for osteo arthritis, neither will work in all cases, but to deny some small place for the value of procaine and lactic acid seems to me to be quite irrational on the known facts

County Hospital, York. EDWARD S VERGETTE

HYPOTHERMIA

SIR,—In his letter about refrigeration anæsthesia last week, Dr Beard refers to having cooled ' two well covered adult females for surgery of the aorta Since, in fact, he means two women it might be better to use this simple Anglo-Saxon description, which incidentally makes it clear that he is not discussing guineapigs Besides, if we stick to the old habit of calling our patients men and women we shall be more likely to regard them as persons rather than as subjects for some of the more hazardous and experimental techniques which have recently made some of your correspondents uneasy about ethical standards in clinical research

London, W1 DAVID LE VAY

HYALINE MEMBRANE IN THE NEONATAL LUNG

SIR,—The discussion that has followed Dr Claireaux's paper of Oct 10 suggests that ideas in this country are following behind those on the other side of the Atlantic A summary by Dr Clement Smith[1] of a symposium in Philadelphia last April on ' hyaline membrane disease (or syndrome) ' has come into my hands during the last few days. His summary seems the most impartial statement of the present knowledge of this condition that I have recently seen, and may be of interest to your readers

"1 The percentage of autopsies showing hyaline membrane formation is highest amongst premature infants, especially those weighing from 1000 to 2000 grams but the incidence is by no means limited to deaths in that gestational age group In our hospital, roughly 50 per cent of the infants who die after premature birth show hyaline membranes and 25 per cent of those dying after full term birth also show them.

"2. The membranes are rarely found if death occurs less than one hour or more than five days after birth It may be that one etiological class of membranes makes up the major group found after death in this age group while another cause may be responsible for those occasionally found in later deaths

"3 Histo-chemical technics are not yet delicate enough to identify the exact chemical composition of membranes beyond the general probability that it is basically protein rather than fat.

"4. The term membrane is perhaps unfortunate in that the same material may apparently occur either as a plug which traps air beyond alveolar ducts with resultant emphysema or resorption atelectasis or as a true membrane spread along the alveolar epithelium.

"5. Pulmonary edema hemorrhage and pneumonic exudates are sometimes found in association with hyaline membrane formation. The group favoured the idea that whether these latter findings were present or not, the membranes tended to be rather generally distributed if found at all and presumably offered significant mechanical interference with respiration

"6. Considerable evidence throws doubts on published theories that aspiration of amniotic fluid is the source of the protein ultimately dehydrated and compressed into these structures. Although membranes have been produced by intra-tracheal injection of human amniotic fluid into excised guineapig and mouse lungs artificially ventilated, the 15 to 20 cubic centimeters of fluid required to bring this about would mean that the infant would have to inspire a relatively tremendous amount of amniotic fluid to bring about a similar train of events. Another difficulty of the amniotic fluid aspiration hypothesis is that it rests largely on the assumption that intra uterine anoxia or similar insult is the stimulus to the inhalation of excess amniotic fluid before or during birth Dr Eastman and other obstetricians who conferred with us at Philadelphia told us that intra uterine anoxia does not at all regularly excite gasping respiratory movement in the human fetus.

The amniotic fluid theory was for these and other reasons left in a rather shaky status but no better contender was forthcoming to take its place Miller's belief that reduced function of the vagus nerve is characteristic of the neonatal period may well be true, but his suggestion that this results in membrane formation at that age was not considered beyond the stage of hypothesis.

"7 Clinically and pathologically there seems to be increasing evidence that many if not all of those infants whose lungs show membrane formation at death may have passed through a phase of relatively adequate pulmonary aeration and some through a phase of actual emphysema Dr Edith Potter prefers the term resorption atelectasis with hyaline-membrane to imply that the atelectasis is not primary

"8 The term hyaline membrane disease is being widely accepted and the belief that it can be clinically diagnosed has led to ideas as to methods of prevention and treatment. Prevention consists according to several in attempts at early and complete drainage of the upper air passages. Most conferees felt that this might be accomplished as well by prompt postural drainage as laryngoscopy and other more dramatic forms of removal. Also prevention of premature or complicated deliveries should reduce frequency of hyaline membrane formation.

"The clinical impression of effective treatment by providing high oxygen supersaturated with water or by the use of wetting agents such as sodium lauryl sulfate has not yet been substantiated To prove the effectiveness of therapy in a condition which can only be diagnosed by autopsy is in itself a baffling problem.

Dr Peter Gruenwald[1] at a Conference in New York on June 5 on the same subject pointed out the non specificity of the membrane and aptly remarked the hyaline membrane of premature babies may be eosinophilic herrings !

Department of Pathology
Children's Hospital,
Western Bank, Sheffield.

JOHN L EMERY

DEXTRAN SULPHATE

SIR,—The introduction by Dr Ricketts and his colleagues (Nov 14) of a synthetic heparin substitute is welcome, but it appears that the question of storage of the substance by the reticulo-endothelial system has not as yet been sufficiently studied. The authors seem satisfied that in case 8 post-mortem sections stained with toluidine blue showed no evidence of storage of material giving a metachromatic reaction. This, however is an unreliable method for demonstrating polysaccharides in tissues unless they are protein bound or otherwise rendered insoluble

In routine hospital practice fixation, mounting of sections and staining are all done in watery solutions, entailing extensive or complete loss of soluble polysaccharides. This possibly explains the failure to demonstrate storage of dextran sulphate in this case

Mowry and Millican,[2] by fixing tissues in and mounting sections from absolute alcohol, and staining by an alcoholic periodic acid—Schiff technique, were able to demonstrate injected dextran in the reticulo-endothelial cells of mice up to 8 months after injection. In view of this, it would seem advisable to re-examine the question using a similar method

The demonstration of storage of the drug would of course, indicate the most exhaustive experiments before it could be advocated for general use.

Chase Farm Hospital,
Enfield, Middlesex.

M. C. BERENBAUM

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[1] Proceedings of a Conference sponsored by Association for the Aid of Crippled Children New York, 1953 pp 13, 10.

[2] Mowry R. W., Millican R. C. *Amer J Path.* 1953 29 523

INCISION FOR ACUTE APPENDICITIS

Sir,—The article by Mr Ewing and Mr Monro (Oct 24) has undoubtedly, *pace* your contributor to In England Now, aroused the interest of a considerable number of your readers May I underline one or two of the points made and add a little to the discussion ?

All experienced abdominal surgeons, I feel, know the advantages of a McBurney's incision in the early case of acute appendicitis On the other hand, in the case where, from the symptoms and signs, one suspects a local or general peritonitis, particularly if the appendix is pelvic in position, the McBurney incision is inadequate and such an incision converted into a muscle-cutting one can be irritating to suture An immediate Rutherford Morison muscle-cutting incision is undoubtedly the better procedure, and, if sutured carefully, layer by layer, with interrupted sutures, heals no less satisfactorily

With regard to the question of drainage, where necessary, may I express admiration for Mr Donald's restraint (Nov 14), and agree entirely with what he says There is, however, no necessity to drain through the wound, a small stab incision between the lower end of the wound and the inguinal ligament, paying due regard to the presence and position of the circumflex iliac vessels, allows a drain to be inserted either down to the pelvis or behind the cæcum, thus achieving adequate drainage and allowing the main wound to heal undisturbed

Workington Infirmary, Cumberland IAN MacKENZIE

Sir,—The correspondence which has followed the article by Mr Ewing and Mr Monro has interested me greatly This is a most important subject

I have come to the conclusion, from routine examination of the abdomen at laparotomy and from 150 peritoneoscopy examinations, that adhesions to the posterior aspect of abdominal scars are the rule rather than the exception It is true they may become less in number with the greater use of non-absorbable suture materials

In a personal series of 65 consecutive operations for intestinal obstruction, 9 (14%) were due to adhesions to the posterior aspect of previous abdominal scars—4 midline, 2 Battle, 1 paramedian, 1 Mayo-Robson (trans-rectus), and 1 grid-iron Need I say more ? The grid-iron scar usually becomes adherent to the cæcum or omentum, seldom giving rise to trouble, whereas the more medially placed scars frequently become adherent to the small intestine

Whittington Hospital
London N 19

W W Davey

Sir,—I wish to add a few personal observations to the lively controversy aroused by Mr Ewing and Mr Monro

In regard to the age old feud between McBurney and Battle, I have, of course, seen herniæ follow both approaches, uncomplicated by clinical sepsis Perplexed as to its occurrence following the muscle splitting incision, I discovered that in two of these cases a "muscle split" had been converted into a "muscle cut' in a third some "cutting" was suggested by the unusually long scar and the mention in the notes of a 'high retrocæcal appendix" Two of the herniæ were inguinal in type

This result is hardly surprising If we agree that the anatomy textbooks are not infallible, then a 2 inch field near McBurney s point is all the more likely to overshadow a nerve The nerve will be displaced with the muscle fibres during the procedure of "splitting," but it will be incapable of stretching and will lie taut across the margin of the incision, where even the smallest cut could sever it

In Battle s approach it seems unkind to suggest that a nerve to the rectus muscle is often cut, but I think that nerve injury may be caused by excessive medial retraction of the muscle In this situation the nerves are rather small, and in the dissecting room I have avulsed them quite easily by medially retracting the rectus Conceivably, avulsion or ischæmic trauma may be similarly produced in the operating theatre

For the midline, paramedian, and Battle fans, I suggest the modified Battle approach In this the anterior wall of the rectus sheath is divided in the line of its fibres in its lateral $^{1}/_{2}$ inch or less, and this incision is extended into the conjoined tendon of the abdominal muscles, lateral to the sheath, for an inch or more Medial retraction of the rectus muscle is slight

This incision, when properly made, is physiologically sound and allows early ambulation, it can be widely extended laterally, it respects the nerves, and it is capable of providing an almost avascular approach And a crease incision, carefully sutured, can be as inconspicuous as any Pfannenstiel after a few months, and it avoids the sustained and devitalising retraction which the latter incision inevitably entails

London, W 2 W H Radley

CORTISONE AND RHEUMATOID ARTHRITIS

Sir,—The letter by Dr Copeman and Dr Savage (Oct 17) reveals the disparity between the earlier hopes and the present estimate of the value of cortisone in rheumatoid arthritis The *fact is that there* is no shortcut to the cure of this disease, but that any results of permanent value can only be obtained slowly

Cortisone therapy, at great expense in material and clinical care, can produce in some patients an initial temporary response, but it is impossible or impracticable to continue such treatment on a large scale for an indefinite time, not only because of the cost, but also because of the undesirable side effects arising from its continued use

If, however, this temporary benefit could be linked with the effect of some other more slowly acting remedy, which could be given for life if need be, there might be some justification for the initial use of cortisone in selected cases Such a remedy exists in the use of an extract of intestinal mucosa, containing as its active agent the group of enzymes known generically as "erepsin"

May I refer your readers to two articles by me on the use of such an extract ?[1] [2] In the second paper I recalled that, of a series of untreated cases of rheumatoid arthritis observed over many years in America, 38% were improved, 15% were in remission, 13% were unchanged, and 34% were worse Taking all my rheumatic cases together, in 1000 cases treated with intestinal extract and observed over a long period, the results were 497 (49 7%) much improved, 407 (40·7%) improved, 89 (8 9%) not improved, and 7 (0 7%) worse. This series included patients who could be regarded as almost hopeless at the outset and who had had a variety of treatments over many years

I do not think that the present intestinal extract that I use is the best which can be obtained, but it does represent a compromise between cost and efficiency, and efforts are being made to improve it The average cost per patient per annum is in the region of £10 for treatment with intestinal extract, and the treatment does not involve much of the doctor's time—an important point in dealing with such a common disease Can Dr Copeman and Dr Savage give us any idea what the average cost of cortisone is likely to be ?

For those who wish to use cortisone in the initial stages I suggest that it might be combined with treatment with an intestinal extract, withdrawing the former as soon as possible but continuing the latter In this event sedatives should be eliminated or reduced to the very minimum so as to allow for an adequate withdrawal of any sedative effect on the secretory activity of the patient's own intestinal mucosa.

One of the most significant facts emerging from the long continued use of an intestinal extract in correct doses, is a slow but extraordinary improvement in the general health of the patient, as well as the slow but definite improvement in the rheumatic condition. After a year or two of treatment many of these patients look five or more years younger and have far more energy

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[1] *Ann rheumat Dis* 1947, 6, 15
[2] *Med Pr* 1953, 229 444

After over twelve years' use of this preparation I am satisfied that it has enabled me to do more good to more patients than any other remedy I have known.

Manchester. ARNOLD RENSHAW

GOOD SENSE ABOUT ANTIBIOTICS

SIR,—We have read, rather belatedly, your annotation of April 25 and although we have not had the opportunity to see the United Bristol Hospitals booklet we do believe that this should be widely circulated.

May we raise a query, however, which seems to be relevant. Although we have made a preliminary survey of the literature covering *the topic of the sensitivity* tests which are suggested for the sulphonamides, we have not yet been able to find a simple method which is satisfactory. On the contrary, some of the methods suggested do not fill the essential requirement of offering any appraisement of the relative activity of the sulphonamides at pH 7·4, which seems to us to be important.

R L HARTLEY
C H BLENKIRON
A S MEATCHEM

Royal Albert Edward Infirmary
and Dispensary, Wigan.

CORONARY HEART-DISEASE IN TRANSPORT WORKERS

SIR,—The statistical analysis by Dr Morris and his colleagues (Nov 21), revealing the different patterns of coronary disease in drivers and conductors, and their different morbidity rates, is surely of great significance.

But I am not at all happy with the authors' assumption that physical activity is a protecting factor for the conductors. One might equally well argue that the mental stress of having constantly to make split-second decisions, involving the possibility of immediate demise not only of himself but of many of his passengers also, is a greater mental stress for the driver than any imposed on the conductor. One can imagine that the secretion of adrenaline among drivers may at times reach very high levels.

It would also be interesting to know how many drivers start their careers as conductors—and how long a driver has been driving.

I well remember twenty years ago discussing the aetiology of coronary disease with a senior member of the profession, and his remark: "I am not so sure the motor-car hasn't something to do with it."

London, W 1 DOUGLAS ROBERTSON

DIARRHŒA AFTER GASTRECTOMY

SIR,—In the case we reported on Sept 19 the patient was stated to have "received water only by mouth and 5% dextrose intravenously." This was a correct factual report. Mr Grant (Nov 21) distorts the facts to fit his theory. He then complains that the literature is confused. What better way of confounding thought and barring progress is there than this?

The assumption that hypertonic dextrose saline solution is generally used is probably now incorrect. At least in this hospital care is taken to give an isotonic solution (4% dextrose in 1/5th normal saline). With this there seems to be much less trouble with venous thrombosis than when 5% dextrose is used.

J E RICHARDSON
D W VERE

Surgical Unit
London Hospital, E 1

SIR,—The diarrhœa following gastrectomy described by Mr Williams and Mr Pullan (Nov 14) develops on the second and third postoperative days. During this period there are definite metabolic changes including a loss of potassium, which in some cases may be severe. In studying cases of hypokalæmia, I have quite often observed diarrhœa which has definitely been secondary to potassium depletion. In fact in some cases the occurrence of diarrhœa has been the first indication of inadequate therapy.

Following gastrectomy one patient developed severe diarrhœa on the fourth postoperative day, and this continued for three days, when the condition became critical. 4 g of potassium chloride was then given intravenously, followed by oral therapy. The diarrhœa ceased within 24 hours of starting potassium therapy.

I suggest that the origin of diarrhœa in postoperative cases may be metabolic in nature and that it may possibly be avoided by maintaining a normal potassium balance as advocated by Ebrill and Naftalin[1] in your columns.

ELSIE W M JOHNSON
Biochemist.

Edgware General Hospital.

TELEVISION AND THE FAMILY

SIR,—Your note last week reviewing our report on Television and the Family suggests that, as the findings of my class are warmly in favour of this form of entertainment, it seems just possible that we are keen televiewers. I can state for myself that I have neither a television set nor do I have a frequent opportunity of viewing. Only two members of my class have television sets. This fact has in no way influenced our findings.

Cheylesmore, Coventry MAX GORDON

Obituary

LANCELOT EDWARD BARRINGTON WARD

K.C.V.O., Ch.M. Edin., F.R.C.S., F.R.C.S.E.

Sir Lancelot Barrington Ward, surgeon to King George VI and since 1952 to the Queen, and consulting surgeon to The Hospital for Sick Children, Great Ormond Street, died at his Suffolk home on Nov 17.

He was born in 1884 at Worcester, the second of the five able sons of the late Canon M. J. Barrington Ward, D.D. Later the family moved to the rectory of Duloe in Cornwall, whence had emanated much of the familiar *Liddell and Scott* Greek lexicon, and in this appropriate environment they grew up nurtured in the classical tradition. Barrington Ward himself was a classical scholar, first at Westminster School, where his health was troublesome, and then at Bromsgrove School, which agreed with him well. Later he gained a classical exhibition at Worcester College, Oxford. Throughout his life his classical education was shown in a masterly command of word and phrase and a handwriting of rare neatness and precision.

[Press Portrait Bureau

But in the end he chose medicine and Edinburgh. As a student he was distinguished not only for the honours degree which he took in 1908 but by his prowess at rugby football. As one of the lightest but certainly one of the best of forwards he was awarded four English international caps. In 1910 he took his Edinburgh fellowship, and the English fellowship two years later. In 1913 he proceeded to the Ch.M. with honours and was awarded the Chiene medal.

His London career began with his appointment in 1910 as a house-surgeon at Great Ormond Street. He was fortunate in the moment of his coming. Under the inspiring leadership of the late George E. Waugh and H. A. T. (now Sir Thomas) Fairbank, the surgery of childhood was arousing interest and study, and Great Ormond Street was attracting young surgeons to the child as well as his fascinating surgical p

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1 Ebrill D, Naftalin, L. *Lancet*, Aug 29 1953

made a peculiar appeal Of such emphatically was Barrington-Ward After his house-surgeoncy he became resident medical superintendent This post, which no longer exists, brought both medical and surgical responsibilities, and was designed to give the holder the comprehensive outlook essential to a children's surgeon In 1914 he was elected honorary surgeon, and appointments to the staffs of the Royal Northern and Wood Green Hospitals soon followed, which offered him full scope for his practice in adults In the development of these two busy and enterprising hospitals he later played a leading part

Soon after the outbreak of war in 1914 he joined for a short time Lady Wimborne's hospital in Serbia On this venture he found meagre scope for his surgical abilities, but he was awarded the Grand Cross of the Order of St Olave and St Sava for his work The experience intensified his abhorrence of war and its wastage, though he later regretted his abstention from the Services

On his return to London responsibilities multiplied apace and the pattern of his busy and successful future was soon established He accomplished a prodigious volume of work, for he was scrupulously loyal to his hospital obligations despite the demands of a widespread and exacting private practice To both he gave his unstinting best, and he got through it all only by care and punctuality in organisation, an unhurried celerity of execution, and a tough physique But he had scanty leisure even for essential rest and recreation, and his contributions to medical journals, though always admirable, were relatively few He did, however, find time in his earlier years to write his classic *Abdominal Surgery for Children* and later he edited the *Royal Northern Operative Surgery* He also contributed to *Garrod, Batten, and Thursfield* and *Hutchison's Index of Treatment* Last year he delivered at the Royal College of Surgeons a masterly Hunterian lecture on Swellings of the Neck in Children He was a past president of the section of pædiatrics of the Royal Society of Medicine, and he was a former president of the Surrey Agricultural Association

In 1918 he operated for appendicitis on the then Prince Albert, and for his services to the Royal Family he was created K C V O in 1935 In 1936 he was appointed surgeon to King George VI, and later he became extra surgeon to H M the Queen.

T T H writes "In the residency of the Edinburgh Royal Infirmary it is—or was—the custom for each house-physician and house-surgeon to record his passage by carving his name on the dining-table On this famous table under the year 1910, among a notable group, stands the name of L E Barrington-Ward In this sign-manual the discerning eye may detect much of the past, present, and future of this young man The carving is in large and conspicuous characters, neat and decisive Even in 1910 one could have surmised a classical training, a hand endowed with no mean dexterity and orderliness of execution, a mind confident and assured, and a personality not unduly modest or retiring The prognosis deducible from that provocative piece of wood-carving has been amply verified Barrington-Ward's natural aptitude for his chosen craft was developed and perfected with assiduous application, and this through the best of all schools of training in gentleness of manipulation and delicacy of touch—children's surgery

"His strength of character was manifested in unwavering confidence in his own ability and in an irrepressible optimism He set himself the highest standard not only in work but in living, nor ever doubted its attainment He accepted good fortune and recognition as his natural and inevitable due and discounted the rest But competence and self-assurance would not alone have brought him that full measure of trust, respect, and affection which were assuredly his Lance, or, if one must be more formal, 'B-W,' was blessed with a magnetic personality Handsome and debonair, courteous and kindly, he invited confidences and inspired instinctive trust His colleagues inevitably turned to him in any personal or family surgical crisis—and how many of us have cause to be grateful to his skill His judgment was as sound as his hands were deft and gentle His equanimity was proof against all the stresses and strains of a surgeon's life, and in the lesser turmoil of committees he was equally imperturbable This quality, along with his wisdom and diplomacy, put him into many committee chairs, and greatly increased the burden of his work

"His home life was always happy and gracious. His tastes were fastidious, he lived generously and always welcomed and entertained his friends genially Yet there was in his general demeanour a dignified, self-contained reserve which was not lightly dispelled, when it was, his friendship was warm, wholehearted, and unassailable For those of us who enjoyed his friendship life can never be quite the same without him He had seemed so enduring and unageing that we cannot but deem his death untimely"

Sir Lancelot married in 1917 Miss Dorothy Anne Miles, who died in 1935, leaving him with three daughters. In 1941 he married as his second wife Miss Catherine Reuter who, with their son, survives him

BERNARD CONSTABLE MAYBURY

M B Lond, F R C S

Mr Maybury, consulting surgeon to St Thomas's Hospital, died on Nov 15 at the age of 65 He was one of the few remaining general surgeons, and his craftsmanship was backed by a profound knowledge of medicine In temperament and outlook he had many of the qualities of the physician

Marcus Adams

The third son of Dr A. V Maybury of Portsmouth, he was educated at Epsom College and St. Thomas's Hospital, and as a student he took almost every prize and medal open to him He was bracketed equal for the scholarship in anatomy in the intermediate examination for the London M B, and he won the Musgrove scholarship and the Cheselden and Treasurer's gold medals at St Thomas's After qualifying in 1909 and graduating M B with honours in surgery in 1910, he held some half-dozen house-appointments at St Thomas's, including that of surgical registrar to Sir George Makins who, with Sir Cuthbert Wallace, became an outstanding influence in his life In 1913 he took the F R C S and was appointed resident assistant surgeon at St Thomas's

The war interrupted his work in London, but during his service as a surgeon at No 9 casualty-clearing station in France and Italy he gained much experience and made many friends It was there work, too, which stimulated his interest in vascular injuries On his return to St Thomas's after the war he was appointed to the staff The new surgical unit had then lately been started under the direction of Sir Cuthbert Wallace, who picked Maybury as the man he needed to work with him Maybury was accordingly appointed deputy director and in due course became surgeon to the hospital, holding his post until February 1948, when he retired on reaching the age of 60 Four months after he left, the retiring age was raised to 65, and everyone at St Thomas's regretted that he, and they, had missed these extra five years

"Maybury was one of those intelligent and efficient people," writes C M P, "who do their work in life with the minimum of self-advertisement He was naturally a self-effacing and reticent man, and I think his close association in work with Sir George Makins and Sir Cuthbert Wallace developed his conservative but critical attitude towards surgical problems He lacked the vigour of body which is often so important an asset to the successful surgeon, but, though plagued by migraine he possessed a toughness of fibre and strong sense of public duty which enabled him to continue work at full pressure until quite recently He was naturally a neat operator and his mastery of the technique of abdominal surgery was recognised by his colleagues from the time of his casualty work in France till his full maturity at

t. Thomas's. His clinical judgment was admirable, nd, though I do not think he was either a successful or popular teacher for the average student, the more dvanced and postgraduate men appreciated his work nd his counsel and many of his patients were to be ound among doctors and their relatives He was not a ood committee-man, but when a matter which concerned im was under discussion, he could be strong and determined in opposition He wrote seldom and then generally nly under pressure from outside His rare contributions o surgical debate were characterised by a full and uthoritative knowledge of the subject at issue. By his assing we lose one of the few remaining generally quipped surgeons of the past era.

R H. O B R, who, after the 1914–18 war, was ppointed the first house-surgeon to the new surgical nit at St. Thomas's, describes Wallace and Maybury as n some ways very similar men They were both ntensely interested in the academic side of surgery nd had an almost morbid dislike of any form of self dvertisement, feeling strongly that there were so many tupid things said by loud mouthed people that it was ll-advised to write or speak until something of importance ould be said This was partly attributable to an innate hyness in both men and because of this they were both ifficult men to get to know well This is the reason why Maybury was not as well known as his merits entitled him to be.

"He was in my opinion the almost perfect surgeon in that he combined in equal measure academic knowledge, nique diagnostic ability, and fine technical achievement Among Thomas's men he was rightly regarded as the most valuable surgical counsellor He was also a magnificent critic and could be guaranteed to see any problem in its right proportions. He published comparatively little but what he did publish was of the highest order Not a strong man physically, he was persistently dogged by ill health which undoubtedly made his task harder He will be remembered as one of the greatest surgeons that Thomas's has produced "

Mr Maybury married in 1930 Isobel Wilson, the daughter of Mr George Lyall, J P She survives him with a son and a daughter

FRANK GEOFFREY HOLMAN
O B E., M.R.C.S

Dr Geoffrey Holman, chief medical officer of the North Thames Gas Board died on Oct. 23 at the age of 44 After qualifying from Guy's Hospital in 1933 he joined the century-old practice of his family in Hampstead. On the outbreak of war he was posted abroad with the R.A.M.C., and most of his war service was spent with field ambulances in Dunkirk, Madagascar, India, and Italy; members of 141st field ambulance will remember him as a shrewd and kindly officer He was promoted to the rank of lieut.-colonel and later he was appointed O.B.E. After the war he did not return to general practice but joined the staff of the North Thames Gas Board, where his sound judgment, unselfish work and genuine interest in people won the respect and affection of his colleagues and patients alike

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Diary of the Week

NOV 29 TO DEC. 5

Monday, 30th

UNIVERSITY OF LONDON
4.30 P.M (London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1) Prof. J R. Squire: Nephrotic Syndrome.

POSTGRADUATE MEDICAL SCHOOL OF LONDON Ducane Road W 12
4 P.M. Dr Brian Ackner Management of Some Common Sexual Difficulties.

Tuesday, 1st

ROYAL COLLEGE OF SURGEONS Lincoln's Inn Fields W C.2
5 P.M. Mr G J Hadfield: Effect of Hormones on Healing (Arris and Gale lecture.)

BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine Keppel Street, W C 1) Dr W D M Paton Anti cholinesterases.

ROYAL SOCIETY OF MEDICINE, 1 Wimpole Street, W 1
5.30 P.M *Sections of Orthopaedics and General Practice.* Dr D T Rowlands, Mr Julian Taylor Mr. Philip Wiles, Mr H E. Harding: Place of Orthopaedic Surgery in Medical Curriculum

KING'S COLLEGE HOSPITAL MEDICAL SCHOOL, Denmark Hill, S E.5
4.15 P.M. Mr V E. Negus Relationship Between Rhinology and Laryngology and Thyroid Gland. (Legg lecture.)

INSTITUTE OF DERMATOLOGY St. John's Hospital, Lisle Street, W.C.2
5.30 P.M. Prof. C. A. Keele Hyperhidrosis.

WEST END HOSPITAL FOR NERVOUS DISEASES, 10 Marylebone Lane, W 1
4.30 P.M Dr Gerald Parsons-Smith: Neurological demonstration.

Wednesday 2nd

ROYAL SOCIETY OF MEDICINE
4.15 P.M. *Section of History of Medicine.* Dr Charles Burns: A Forgotten Psychiatrist—Baron Ernst von Feuchtersleben M.D (1833). Prof. F Wood Jones Strange Career of an Anatomist.
8 P.M. *Section of Surgery* Mr F J Gillingham, Mr W S. Lewin, Miss D J Beck: Head Injuries in Civil Practice

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE 28 Portland Place, W 1
3.45 P.M. Sir Harold Whittingham Hygiene and Sanitation in Aviation.

INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr H. Haber Bullous Eruptions of Skin.

INSTITUTE OF UROLOGY, 10 Henrietta Street, W C 2
5 P.M. Mr F R. Kilpatrick Tuberculosis of Renal Tract.

MANCHESTER MEDICAL SOCIETY
4.30 P.M. (Medical School University of Manchester) *Section of Medicine.* Dr A. Morgan Jones: Coronary Disease.

MIDLAND MEDICAL SOCIETY
8.15 P.M (151 Great Charles Street, Birmingham 3) Mr Lawrence Abel: Present Position of Cancer Problem.

MEDICO-CHIRURGICAL SOCIETY OF EDINBURGH
8.30 P.M. (Royal College of Surgeons, Nicolson Street.) Dr J P Stewart, Dr M. Z. Kawa: Further Observations on Effect of Cortisone and A.C.T H in Treatment of Allergic Rhinitis.

Thursday 3rd

BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine.) Dr R. M B. MacKenna Scientific Approach to Dermatology

ROYAL SOCIETY OF MEDICINE
5 P.M. *Section of United Services.* Group-Captain R. L. Soper Air Transport of Poliomyelitis Cases in Mechanical Respirators. Squadron Leader C. B. Wynn Parry: Aspects of Rehabilitation in Royal Air Force.
8 P.M. *Sections of Neurology and Paediatrics.* Mr G I. Scott, Mr J H Doggart, Dr S P Meadows, Dr J G Greenfield: Neuro-ophthalmological Aspects of Failure of Vision in Children

INSTITUTE OF LARYNGOLOGY AND OTOLOGY
5.30 P.M (Royal College of Surgeons, Lincoln's Inn Fields, W C.2) Dr Michael Ward: Ascent of Mount Everest—Medical Problems

CHADWICK LECTURE
5 P.M. (Wright Fleming Institute, St. Mary's Hospital, Paddington W 2) Prof. B W Windeyer: Radiotherapy in its Relation to Dermatology (Malcolm Morris lecture.)

LIVERPOOL MEDICAL INSTITUTION 114 Mount Pleasant, Liverpool, 3
8 P.M Symposium on Pathology of Tuberculosis.

Friday 4th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P.M. Dr R. G Macfarlane Marrow Puncture

ROYAL SOCIETY OF MEDICINE
10.30 A.M. *Section of Otology* Mr Kenneth Harrison Ramsay Hunt Syndrome.
3 P.M. (Royal College of Surgeons, Lincoln's Inn Fields, W C.2.) *Section of Laryngology* Mr Munro Black, Dr B T Davies: Keratoses of the Larynx.
5 30 P.M. *Section of Anaesthetics.* Dr A. J W Beard Antihistamines in Anaesthesia. Dr A. A Juvenelle: Experiments with Deep Hypothermia. Dr D G Melrose Applications of Heart lung Machine in Man.

INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr R. T Brain: Diseases of Children.

HEBERDEN SOCIETY
3.30 P.M. (Royal College of Surgeons.) Sir Russell Brain, P.R.C.P Spondylosis—the Known and the Unknown. (Heberden oration.)

WHIPPS CROSS HOSPITAL MEDICAL SOCIETY Whipps Cross Hospital E.11
8.30 P.M. Proposer Mr George Benson M.P Opposer Dr W J O Donovan Corporal Punishment has no Place in the Penal System of an Enlightened Society

LEEDS AND WEST RIDING MEDICO-CHIRURGICAL SOCIETY
7 30 P.M. Prof. Charles Wells The Suprarenal Gland.

Saturday, 5th

MIDLAND TUBERCULOSIS SOCIETY
8 15 P.M. (151 Great Charles Street, Birmingham 3) Prof T Pilcher Bronchiectasis in Children.

Notes and News

SMOKE ABATEMENT

SPEAKING in Manchester on Nov 23, Mr Arnold Marsh, general secretary of the National Smoke Abatement Society, said that for many years a patient, guerilla like campaign against smoke had been waged by a handful of partisans Now, because of last December's tragedy in London, a full-scale counter attack was in train, and although the partisans were still few they were at least being encouraged by a public that had suddenly become aware of the deadly enemy in their midst Such a great surge of public interest could, however, create its own difficulties, and two important factors were in danger of being overlooked. First, the occasional lethal smog is probably less damaging in its effects and cost than the normal smokiness of the atmosphere, which insidiously undermines health Secondly, though sulphur dioxide is certainly the most acid and corrosive part of the pollution, the smoke in itself affects the health of town dwellers by screening them from the sun In the winter months up to two thirds of a city's natural light may be cut off by the overhanging pall of smoke Though it must take a long time to get rid of even a part of the sulphur dioxide, to get rid of smoke alone, which could be done quite soon, would reduce the dangers and costs of air pollution to a fraction of what we now experience Meanwhile, Mr Marsh added, the smoke abatement movement is still struggling along on a shoestring "I sometimes wonder, when vast sums are being raised, or are coming out of taxes, to restore some famous building from the ravages of smoke, whether a small percentage—just a crumb—might not also be devoted to efforts to stop it from happening again "

SCOTTISH HOSPITAL ENDOWMENTS

THE Scottish Hospital Endowments Commission, presided over by Sir Sydney Smith, have issued a memorandum describing the principles on which they propose to distribute the £13 million of endowments to hospitals in Scotland. They propose that every hospital board of management in Scotland should have at least £2 per bed a year to provide for patients and staff amenities, such as additional furnishings and wireless sets, which cannot always be charged to the National Health Service Where a board of management has at present no endowments or insufficient endowments, the commission will transfer funds to it from other boards in the same general area Each board will be left free to perpetuate by name any endowments which it considers should be commemorated A few endowments, the commission think, should be retained for specific purposes, such as funds for nurses' prizes.

Where a board has sufficiently large endowments the commission will transfer part to the Scottish Hospital Endowments Research Trust set up this year by the Hospital Endowments (Scotland) This Act allows for the transfer of endowments to provide the Trust with an income of up to £120,000 a year to further medical research. Boards are also free to use their endowment funds for research

CLINICAL ORTHOPÆDICS

IN the first issue of a new periodical, *Clinical Orthopædics,*[1] the editor in-chief, Dr A F De Palma, says "Most of us are keenly aware of the need for additional outlets for material of orthopædic interest , also, it is generally known that the existing journals are swamped with good material which because of the lack of space is denied publication In addition, the English speaking countries do not have an organ capable of providing avenues of expression for the ever increasing subdivisions of orthopædic surgery and the allied specialities Finally, no concerted efforts have been made by the orthopædic group as a whole to keep the general practitioner and the surgeon in allied fields abreast of the rapidly growing scope of orthopædic surgery " His object therefore is to carry the news "not only to orthopædic surgeons and traumatic surgeons, but also to all those in the allied specialities and above all, to the general practitioner "

Surprisingly enough, the first issue is a book of nearly 250 pages including a 12 page index which seems unnecessarily detailed for what sets out to be a journal The plan is to publish two volumes a year, each divided into two parts. The first part is to be devoted to a single subject (the first issue deals with some problems of orthopædics in children); and the second will contain miscellaneous articles.

These objects are impressive in their scope, and are apparently intended to appeal to a wide range of doctors But, in this country at any rate, few general practitioners would have the time or inclination to read such an extensive publication, much of which is of no practical interest or value to them Moreover, much of what is intended for the general practitioner is of no great interest to the orthopædic surgeon, it is more on the lines of what is being done so well already in this country in the various types of refresher course Nevertheless, tastes differ, and it may well be that in the United States the general practitioner is expected to have a more detailed knowledge of the practical and theoretical aspects of orthopædics

The standard of the articles in the opening volume is on the whole high. In the first section most of the articles are written for general practitioners, and it may be questioned whether it helps them to read more than one article on the same subject, particularly when these give conflicting viewpoints which are really only the concern of the specialist. But, whatever the verdict of the general practitioner, the orthopædic surgeon will find plenty to interest him.

A JOINT BED BUREAU

WHEN the National Health Service was started almost all the mental deficiency hospitals which had been administered by the Lancashire Mental Hospitals Board to provide for the needs of Lancashire and Cheshire and the county boroughs fell within the Manchester Regional Hospital Board area. The result has been that the Manchester board have over 6000 beds for mentally defective patients and the Liverpool Board a little more than 600 In 1948, many patients in the institutions in the Manchester region had been admitted from the Liverpool region and during the past five years the Manchester board have continued to place beds at the disposal of the Liverpool board It has now been agreed that all applications for the admission of mentally defective patients from local authorities within the areas of both boards will be referred to a joint bed bureau at the offices of the Manchester board The bed bureau will maintain waiting lists of patients and the priority for admission will be determined by collaboration between Dr G R Pile, regional adviser in mental deficiency to the Manchester board, and Dr N Fraser MacKenzie, regional adviser to the Liverpool board In this way, as suitable vacancies arise, patients will be admitted in accordance with their needs and it will be possible for the boards to give assurance that the most urgent cases will receive the earliest attention

TUBERCULOSIS IN DECLINE

EVERY second that passes converts live truth into dead history, and we all know that history is more a matter of opinion than of fact Just now we are watching a decline in the death rate from tuberculosis, and it is pleasant to believe that medicine and public health have had some hand in bringing it down. Yet as Dr Iago Galdston recalled last year,[1] the decline began in the first half of the nineteenth century, long before we knew anything about the tubercle bacillus, or took any special measures against it, and he quoted the remark of René J Dubos, made in 1951, that "Neither the discovery of the tubercle bacillus, nor the growth of the sanatorium movement, nor the organisation of the antituberculous associations, nor the introduction of pneumothorax therapy, seem to have affected markedly the shape of the curve." Moreover, the mortality from some other diseases—notably pneumococcal pneumonia, bronchitis, Bright's disease, scarlet fever, and measles—has also declined since the same date, which led Brownlee to conclude that "a considerable part of the decline of tuberculosis in recent years is in line with the biological properties of disease in general, and has little to do with hygienic conditions "

But there are good grounds for distrusting these gloomy opinions about the history of tuberculosis, as Dr Galdston points out It may be true that tuberculosis has had its ups and downs in the past, and that we are fortunate to be coinciding with a down, but the curve is too general to take account of those minor deviations from the mean in which circumstances seem, for good or ill, to have taken a part. Thus, Negroes are particularly susceptible to tuberculosis, ut in Charleston, South Carolina, between 1822 and 1830, the mortality rate for both Whites and Negroes, though high—round about 450 per 100,000 living—was equal. By 1865–74 after the Civil War when the freed Negroes suffered sorely from want, the rate for Whites had fallen to 200, but that for Negroes remained at over 400 During the succeeding decades the rate for Whites remained fairly steady while the rate for Negroes rose until in 1900 it was 675 Again in New York in 1950, when the tuberculosis death rate for Whites was 22, and the case-rate 80 per 100 000 population, the comparable rates in Harlem, the Negro quarter were 361 and 109 In the heart of this congested area the rates were even higher: 470 and 153. Thus if we cannot speak authoritatively of the effect of public-health measures and better housing on the downs of tuberculosis, we can be confident that the lack of them affects the ups : as Dr Galdston says, We know that misery deprivation poverty overwork, always have been reflected in a rise of the tuberculosis mortality He argues that tuberculosis is primarily a state of being and only derivatively a disease. The tubercle bacillus is always with us, but whether it can prevail against man and produce disease or remain in some form of symbiotic balance depends on man s state of being—which in turn depends on man s own knowledge awareness, conscience and wisdom—how in a word, he manages his social and individual affairs.

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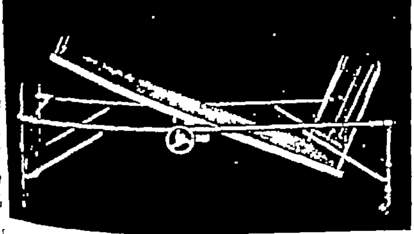
[1] Published by J B Lippincott Bedford Street London W C 2 —Single copies 48s , to subscribers 40s

[1] On the Epidemiology of Tuberculosis Lecture to the Michigan Tuberculosis Association, June, 1952 A Christmas Seal Publication. Pp 16

In the last few years our knowledge has been widened by the discovery of new drugs, and we have seen a rapid decline in mortality from tuberculosis, not only in Great Britain but all over the world. Yet as the annual report for 1952–53 [2] of the National Association for the Prevention of Tuberculosis puts it we are really interested more in lives than deaths and there is no evidence that the incidence of fresh cases of tuberculosis is declining—rather the reverse In England and Wales we are still getting some 45 000 new cases a year The N.A.P T being deeply concerned with the preventive ideal, has contributed to publicity for mass-radiography issued leaflets about B C G., published material of interest to doctors in the *N.A.P T Bulletin*, arranged exchange scholarships for doctors from overseas, organised conferences on various aspects of tuberculosis work, provided scholarships to tuberculosis nurses wishing to train for the post of nurse teacher financed investigations into reablement programmes, kept touch with interested people and fellow organisations in the Commonwealth, and distributed much propaganda The funds for this work come largely from the sale of the N.A.P T Christmas seals, which are now so well known as to need no introduction This year the coloured design shows a horn of plenty spilling gifts; and the N A.P T in expectation of a record sale of seals, have printed 100 million of them. At $^1/_2d$ each they have already raised hundreds of thousands of pounds for this good cause They can be bought in sheets of 100 at 4s (which means there are 4 thrown in for luck) and there are also Christmas cards in two designs at 6s a dozen. Both may be had from the Duchess of Portland chairman, N.A.P T Tavistock House North, London, W C 1

NEW TILTING BED

THE Sidhil Dewhurst bed, illustrated here, is intended for postural drainage With it, greater tilt is possible than with blocks under the feet at one end and the centre of gravity is not raised as it is with blocks. The tilting device, which works on a quadrant-and worm arrangement, is easily operated. The bed is held stationary by two wood stump feet at the foot end It has been designed by Mr Harry Dewhurst, supplies officer of the Burnley and district hospital group in association with the manufacturers, Messrs. Siddall & Hilton Ltd. Centre Mills, Sowerby Bridge, Yorkshire



University of Cambridge

On Nov 14 the following degrees were conferred:

M.A —F W Campbell.
M.B B Chir — R. J Hutchinson.
* By proxy

University of London

The title of reader in entomology as applied to hygiene has been conferred on Mr J R Busvine D.SC., in respect of the post held by him at the London School of Hygiene and Tropical Medicine.

University of Leeds

Dr D G F Harriman has been appointed lecturer in neuropathology in the department of pathology

University of Sheffield

Dr T J Rendle-Short has been appointed lecturer in child health Dr K S. Holt tutor in child health, and Dr D H Anderson part-time clinical teacher in chest diseases

Dr Irving Gordon, of the New York State Department of Health, has been appointed a visiting senior lecturer in bacteriology during his visit to the university this session

University of Birmingham

The university is appealing for £500 000 which is needed during the next seven years for research and education Last year the annual costs were £1$^1/_4$ million towards which the Government gave £800 000 and endowment and other resources are not enough to bridge the gap

In supporting the appeal Dr A. P Thomson vice-principal of the university cited as examples of research that might be held up for lack of funds, work on a substitute for blood needed for transfusions the investigation by chemical dissection of the brain, of breakdowns in workers caused by nervous stress, and the causes of morbidity Money is also needed for building.

Royal College of Surgeons in Ireland

On Nov 20 the following were admitted to the fellowship:

E. G Leahy and Alexander McCallister

Society of Apothecaries of London

Dr H. Seaward Morley master presided at a recent meeting of the court of assistants at which Dr J P Hedley was reappointed as the society's representative on the General Medical Council

The following were elected to the livery:

I M. Jackson, H. L. Shepherd, B G. Parsons-Smith G E. W Wolstenholme V W Dix, G L. M. Swyer, T Holmes Sellors, A. H Douthwaite, C. E. W Wheaton B R. Schlesinger J J Keevil, Donough O Brien, T S. Leedham, R. Bodley Scott, Ursula Shelley Sir Stewart Duke Elder, G R. H. Wrangham, C. F T East, H P Winsbury White, G H. Macnab J H. Gurney-Smith, C. A. Keele L. R. Broster H F Turney A. G. Boyle, H H. F Barns, A. R. H. Hicks, Selwyn Taylor R. H. Franklin, K. G Tuckwell, P A. Tyser G A. Mason H B S. Warren, P Ll. Blaxter J A. E. Young

The following were admitted to the freedom of the society:

S. H. Wass, M M. Scott, C. F Harris, H G. E. Arthure [illegible] O Donovan, Samuel Oram, R. H. Parry H R. Hayman, [illegible] Thorn F H. Young G B Woodd Walker C. S. Cane.

The following were bound apprentice:

Nicholas Tyrrell Evans to W S. C. Copeman [illegible] D P Lambert.

W A. W Dutton passed the examination [illegible] midwifery

The following having completed the [illegible] been granted the L.M.S.S.A.:

C S Chou, R. L Cort, W C. [illegible] Nasr W P N Moore, A. C Parry P [illegible] J D Van Asswegan, D S. Pickup.

Faculty of Homœopathy

A meeting of the faculty [illegible] Homœopathic Hospital [illegible]

European Society of [illegible]

This society will [illegible] July 9 and 10. [illegible] of the Extremities, [illegible] Phlebitis. [illegible] Slessor Department of Surgery, [illegible] Edinburgh [illegible]

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[2] Leadership Against Tuberculosis. N A.P T., Tavistock House North, Tavistock Square London, W C.1 Pp 64

Middlesex Hospital

Prof Brian Windeyer has been appointed dean of the medical school in succession to Sir Harold Boldero, who will retire next year after holding office for 20 years.

Heberden Society

Sir Russell Brain, P.R.C.P., will deliver the Heberden oration on Friday, Dec 4, at 3 30 P.M., at the Royal College of Surgeons, Lincoln's Inn Fields, W C 2 He is to speak on Spondylosis—the Known and the Unknown

Journal of Embryology and Experimental Morphology

The annual meeting of the editorial board of this journal will be accompanied by public scientific sessions at which papers by members of the board will be read and discussed These will be held in the department of anatomy, University College, Gower Street, London, W C 1

The Young Worker

The department of education of the University of Oxford is holding a conference at Manchester College, Oxford, from April 3 to 9, on the Young Worker Education for Human Relations Further particulars may be had from the conference secretary of the department, 15, Norham Gardens, Oxford

Tuberculosis Educational Institute

Clinical courses for doctors will be held at Sully Hospital, Glamorgan (Jan. 20–21), at King George V Hospital for Diseases of the Chest, Godalming (March 3–5 and Sept 29–Oct 1), Red Cross Sanatoria of Scotland (April 7–9), Cheshire Joint Sanatorium, Market Drayton, Salop (April 28–30 and Oct. 27–29) Further information may be had from the secretary of the institute, Tavistock House North, Tavistock Square, London, W C 1

Absent from School

At a Nottingham court on Nov 17 parents who had been summoned for not sending their children to school alleged that their doctor had refused to issue medical certificates for sickness An education department officer explained that the case was not an isolated one Doctors who withheld certificates usually advised the parents to tell education officials to contact the doctor if there were any inquiries But there were 47,000 children in the city Some were away every day, and the department could not keep interrupting a doctor's busy surgery

Centre for Spastic Children

Under the sponsorship of the No 4 (Chelsea) Group Hospital Management Committee a day centre for spastic children under the age of five or six is to be opened in part of the Cheyne Hospital for Children, Cheyne Walk. To begin with about 24 children will be taken, but it is hoped to expand the work later In the meantime a group of people, called the Friends of the Spastic Centre, have been formed Those who are interested are asked to attend a meeting at the Chenil Galleries, King's Road, Chelsea, on Monday, Dec 7, at 3 P.M.

Society of Chemical Industry

At the next meeting of the microbiology group of this society to be held on Thursday, Dec 3, at 6 15 P.M., at 11, Chandos Street, London, W 1, Prof M Stacey, F.R.S., Mr A E James, Dr F Fletcher, Mr A R Lockwood, and Mr A. W Wilkinson, F.R.C.S., will deliver papers on Dextran

The society's food group (nutrition panel) is to hold the second meeting of its series on Nutritional Reappraisals on Wednesday, Dec 9, at 11, Chandos Street, London, W 1, at 6 30 P.M., when Dr R Passmore will speak on Some Recent Investigations of Human Calorie Requirements

Half a Bus

The physiotherapy department of Wolverhampton Royal Hospital has installed half a bus, complete with staircase, on which patients may practise getting up and down stairs and accustom themselves to normal travelling

Films on Psychology and Psychiatry

The Scientific Film Association has published a catalogue of 107 films on psychology available in this country The catalogue is divided into the following sections developmental psychology, educational psychology, testing techniques, industrial and applied psychology, animal and experimental psychology, abnormal psychology and psychiatry, and juvenile delinquency Copies may be had (7*s* 6*d*. plus 7*d* postage) from the association, 164, Shaftesbury Avenue, London, W C 2

World Veterans Federation

The rehabilitation peace prize of this federation has been awarded to Dr Ludwig Guttmann, director of the spinal injuries centre at the Ministry of Pensions Hospital, Stoke Mandeville, Bucks

Assay and Detection of Pyrogens

A symposium on this subject is to be held by the Pharmaceutical Society and the biological methods group of the Society of Public Analysts at 2 30 P.M. on Friday, Dec. 11, at University College, Gower Street, London, W C 1 The symposium is open to all who are interested in the subject, and summaries of the papers may be had from Mr K. R. Capper, editor of scientific publications of the Pharmaceutical Society, 17, Bloomsbury Square, W C 1

Multiple Sclerosis Society

The inaugural meeting of this society was held in London on Nov 18 The chief aim of the society is to help patients with this disease to be useful citizens rather than invalids. Members of the society will visit patients to give advice, companionship, and, when necessary, financial help Local groups of the society are to be formed, and further particulars may be had from the secretary of the society, 9, Grosvenor Crescent, London, S W 1

Medical Memorials

On Nov 7 a new outpatient department at Trowbridge and District Hospital was formally opened as a memorial to John Levis, consulting surgeon to the hospital from 1919 until his death in 1943

A plaque in memory of Alexander Mitchell, consulting orthopædic surgeon to Aberdeen Royal Hospital, has been unveiled at Fyvie Cottage Hospital, Aberdeenshire.

Medical Training in the East

The governments of Malaya and Singapore have appointed a committee to inquire into " the future needs of university medical education, including education in dentistry and pharmacy, in Singapore, the Federation of Malaya, and Borneo, and to advise on the provision and siting of the facilities necessary to meet those needs " The members of the committee, Sir David Lindsay Keir (chairman), master of Balliol College, Oxford, Dr J H Biggart, professor of pathology and dean of the faculty of medicine, Queen's University, Belfast, and Mr T P Kilner, Nuffield professor of plastic surgery in the University of Oxford, leave by air for Singapore on Nov 22

CORRIGENDUM *Myxomatosis*—In our annotation (Nov 14 p 1031) we said that hundreds of millions of rabbits had died in Germany and the Low Countries In fact, the epidemic has only lately reached these countries, and, though the total is certainly to be reckoned in hundreds of millions, the deaths so far have been mainly in France The latest news (*Manchester Guardian*, Nov 21) is that the disease is spreading in Western Germany

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Surgeon Commander R. M. Coplans, R.A.N has been appointed honorary physician to the Governor General of Australia.

Births, Marriages, and Deaths

BIRTHS

RUGG GUNN —On Nov 20 to Patricia, wife of Surgeon Commander M A. Rugg Gunn M.D., M.R.C.P R.N —a son.

Appointments

CAMERON MARGARET, M B Glasg, D.P H asst. M.O., Inverness County Council.

* MICHELL, E P G, M B. Camb M R.C.P D C.H. house physician, The Hospital for Sick Children Great Ormond Street, London.

THORP T A J, M B Manc D.P H M O school health service Manchester Education Committee

WEIR, J G M.A. M.B Aberd registrar in psychiatry, Addenbrooke's Hospital and Fulbourn Hospital, Cambridge

Colonial Service

ANDERSON R. E, M B St And, D.P H D T M & H. D.D.M.S., Federation of Malaya.

BENDER K. B, M.R C.S government M O, British Guiana.

BEVAN R. G B M.B St And M O, British Solomon Islands Protectorate

CLAPHAM L J, M.B Lond, D T.M. & H., D.P.H. D.M.S, North Borneo

RUNCIMAN C M B M O Tanganyika.

STRUDWICK R. H, M B Birm M.O Hong Kong

* Amended notice

NTIBIOTIC AND CHEMOTHERAPEUTIC AGENTS IN THE TREATMENT OF NFANTILE DIARRHŒA AND VOMITING

PORT BY A WORKING PARTY * ESTABLISHED BY THE TIBIOTICS CLINICAL TRIALS (NON TUBERCULOUS CONDI ONS) COMMITTEE OF THE MEDICAL RESEARCH COUNCIL

This paper describes the conduct and results of ntrolled therapeutic trials designed to investigate the nical effects of the oral administration of aureomycin, oramphenicol, and sulphadiazine on infantile diar ea and vomiting, excluding salmonella and shigella ections. The work was undertaken at ten separate ntres in Great Britain

mingham	Children's Hospital.
inburgh	Royal Hospital for Sick Children and the City Hospital.
rpool	Alder Hey Children's Hospital.
ndon, G O.S.	The Hospital for Sick Children Great Ormond Street.
ndon, Q E.H	Queen Elizabeth Hospital for Children
ndon, S.A H.	St. Ann's General Hospital.
nchester	Booth Hall Children's Hospital and the Duchess of York Hospital for Babies.
wcastle upon Tyne	General Hospital
effield	Children's Hospital and City General Hospital.
thampton	Children's Hospital and Public Health Laboratory

General Description of Investigation

The investigation began in March, 1950 and continued r about two years. During the first eight months four the centres were engaged on trials of aureomycin and ve on trials of chloramphenicol One of the centres iverpool) using chloramphenicol then began a trial aureomycin also Two months later another centre ondon, S.A.H) not previously participating in the vestigation, began a trial of aureomycin At all the entres the progress of a series of cases treated with he drug under trial was compared with that of a ncurrent series of control cases

The treatment of control cases needs some comment t this stage of the report When the investigation as planned, it was intended that control cases would ceive no antibiotic or chemotherapeutic agent by mouth, at least during the first week of treatment. It later became evident that this intention would be imperfectly realised, since ethical considerations arising from past experience of the treatment of infantile diarrhœa and vomiting influenced the practice at different centres. At most of the centres antibiotic or chemotherapeutic agents were given by mouth to control cases only in occasional circumstances—e g when an infant was not responding to routine methods of treatment and it was considered unjustifiable to withhold additional therapy At one of the centres using aureomycin (London, S.A.H) all the severely ill patients, both aureomycin treated and control, were given sulphadiazine by mouth from the outset. At another centre using aureomycin (London, G O S) a high proportion of controls were given either sulphadiazine or chloramphenicol by mouth.

The implications of these variations in treatment are discussed below, but at this point it is necessary to state that at one centre (Edinburgh) where chloramphenicol was being tried the oral administration of sulphadiazine formed part of the routine method of treatment of control cases From the results obtained at this centre during the first year of the investigation it became evident that sulphadiazine-treated cases would need separate consideration. Accordingly the scope of the investigation was extended and further trials were planned with the object of comparing the therapeutic effects of sulphadiazine with those of chloramphenicol in concurrent series of cases.

All the cases included in the investigation fell therefore, into four main treatment groups aureomycin treated (A) chloramphenicol treated (C) sulphadiazine-treated (S) and controls (R) Table I shows the treatment groups adopted at the various centres and the duration of each trial from the admission of the first to the admission of the last case in the respective series.

Design and Conduct of Trials

TYPES OF CASE INCLUDED

Throughout each of the trials all infants coming under treatment for diarrhœa and vomiting at the centres concerned were included in the investigation, except those who were assessed within twenty four hours of the start of treatment as having no diarrhœa and those who at the start of treatment were aged 1 year or more or fully breast fed or found to have gross structural abnormality or evidence of gross organic disease.

Infants included in the investigation and later found to have either salmonella or shigella infections were excluded from the final analysis of results Infants with parenteral infections were included in the trials and in the final analysis of results, except those who had severe parenteral infections—e g, meningitis, or pneumonia—as their primary disease

INITIAL CLASSIFICATION AND ALLOCATION TO TREATMENT GROUPS

Before allocation to a treatment group each case was classified according to age and to severity of illness The cases were classified according to age at the time of entry to the trial as follows: (1) aged less than 1 month (2) aged 1–5 months and (3) aged 6–11 months

The initial severity of the illness in each case was assessed within twenty four hours of entry to the trial. A case was classified as severe if considered to need parenteral administration of fluid otherwise it was classified as mild.

All the cases included in the investigation were therefore classified within twenty four hours of entry into one of six age and severity groups Throughout each trial successive cases in each age and severity group were allocated in rotation to the appropriate treatment groups as shown in table I except at one centre (London, S.A.H) where a modified random allocation was made (see below) Minor differences in the numbers of cases appearing in concurrent treatment groups were due partly to errors of allocation in the early stages of the investigation and partly to subsequent exclusions because of either salmonella or of shigella infections discovered after entry

ROUTINE TREATMENT

Apart from the oral administration of antibiotic or chemotherapeutic agents each centre continued to use its own routine methods of treatment. These methods differed in detail but the basic principles were similar at all ten centres.

Mild cases were treated with electrolyte solutions with or without the addition of glucose, by mouth for twenty four hours, in quantities adequate to meet a daily fluid requirement of 2½–3 oz per lb of body weight. Dilute

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* The members of the Working Party were Dr R H. Dobbs (chairman) Dr M. B Alexander, Prof. N B Capon Dr Richard Doll, Dr S. A. Doxiadis, Prof R W B Ellis Prof Wilfrid Gaisford Dr J Gerrard Dr R. R. Gordon Dr J L. Greaves, Dr E G Hall, Dr A. Holzel, Dr R. I. Hutchinson Prof. R. S. Illingworth, Dr G M. Lowdon Dr M. M. McNeill, Dr G A. Neligan Dr George Ormiston Dr K. B Rogers, Dr Bernard Schlesinger, Prof J M. Smellie Sir James Spence, Dr R M Todd Dr R. G Welch Dr Joyce Wright Dr Winifred Young and Dr A. T Roden (secretary).

6797

TABLE I—TREATMENT GROUPS AND DURATIONS OF TRIALS AT THE VARIOUS CENTRES

Centre	Trial no	Treatment groups	Duration of trial
Birmingham	1	C R	April, 1950–March, 1951
Birmingham	2	C S	August, 1951–March, 1952
Edinburgh	1	C S	April, 1950–August, 1951
Edinburgh	2	C S	September, 1951–March, 1952
Liverpool	1	C R	March, 1950–October, 1950
Liverpool	2	A C R	November, 1950–May, 1951
Liverpool	3	C S R	June, 1951–March, 1952
London, G O S	1	A R	April, 1950–May, 1951
London, G O S	2	C S	June, 1951–March, 1952
London, Q E H	1	C R	April, 1950–May, 1951
London, Q E H	2	C S R	June, 1951–March, 1952
London, S A H	1	A R	January, 1951–July, 1951
Manchester	1	A R	April, 1950–May, 1951
Newcastle	1	C R	April, 1950–April, 1951
Sheffield	1	A R	April, 1950–May, 1951
Southampton	1	A R	April, 1950–May, 1951
Southampton	2	C S	August, 1951–March, 1952

A, aureomycin.   R, routine (control)
C, chloramphenicol   S, sulphadiazine

milk feeds were then begun and their strength gradually increased until, by the fifth to the eighth day of treatment, depending on the practice at the different centres, feeds were offered sufficient to supply the full daily requirement of 50 calories per lb. body-weight. The type of milk feeds offered and the usual rate of increase in their calorie content varied at different centres.

Severe cases were treated by continuous intravenous infusion of glucose and electrolyte solutions with the addition, at some centres, of dilute human serum or plasma, in quantities adequate from the start of treatment to supply the total daily fluid requirement and to correct dehydration. Oral administration of clear fluid was begun from twelve to twenty-four hours later. Dilute milk feeds were then introduced and their strength gradually increased. Intravenous therapy was continued until oral fluids were well tolerated.

DOSAGES OF TRIAL DRUGS

Dosages of the trial drugs were based on the infant's body-weight on the day of entry to the investigation and were calculated, for each infant in the appropriate treatment groups, according to the following scales:

(A)	aureomycin	75 mg. per lb. a day
(C)	chloramphenicol	75 mg. per lb. a day
(S)	sulphadiazine	125 mg. per lb. a day

The dosages of aureomycin and of chloramphenicol were chosen at the outset of the investigation, when there was little to guide the Working Party except that some of its members had previously given the drugs in these quantities without apparent ill effect. So that the results of treatment might remain comparable, no alteration in dosage was made throughout the investigation.

The drugs were given by mouth in divided doses, at intervals not exceeding six hours, for seven days. Administration was begun as soon as a sufficient time had elapsed to enable the initial assessments to be made, and in no case later than twenty-four hours after entry to the trial. The drugs were dispensed in syrup or some other sweet-flavoured vehicle. Supplies of aureomycin in the form of 250 mg. capsules were found not to be particularly convenient for the measurement of individual doses according to the scale chosen by the Working Party. Otherwise no difficulties were experienced either in dispensing or administering the drugs.

CLINICAL RECORDS

A clinical summary was made of each case included in the investigation to show:

(1) The age and severity classification.

(2) Other criteria chosen for subsequent analysis of the initial comparability of the different treatment groups:
  - (*a*) Source of cases—i.e., from institutional or from domiciliary practice.
  - (*b*) Duration of diarrhœa before entry to the investigation.

(3) The treatment group.

(4) Criteria of clinical progress after entry to the investigation:
  - (*a*) Death or survival.
  - (*b*) Duration of diarrhœa. The interpretation of this criterion—i.e., the time at which the stools became normal in amount and consistence—was left to the individual judgments of the physicians in charge of the cases at each centre.
  - (*c*) Time to clinical recovery. It was agreed by all concerned that clinical recovery implied a satisfactory general condition, stools of normal consistence, and ability to tolerate an adequate diet. At some centres gain in body-weight was included in the assessment of clinical recovery.
  - (*d*) Number of mild cases becoming severe—i.e., subsequently needing intravenous therapy.
  - (*e*) Relapses of diarrhœa. Recurrences of diarrhœ not later than fourteen days after clinical recovery

TABLE II—NUMBER OF CASES IN EACH TRIAL AND DISTRIBUTION OF CASES IN TREATMENT, SEVERITY, AND AGE-GROUPS

Trial	Total no. of cases	Distribution of cases																							
		Treatment group				Severity								Age group											
		A	C	S	R	Mild				Severe				Less than 1 month				1–5 months				6–11 months			
						A	C	S	R	A	C	S	R	A	C	S	R	A	C	S	R	A	C	S	R
Birmingham 1	73		37		36		16		15		21		21		1		2		28		26		8		
Birmingham 2	26		12	14			10	12			2	2			1	1			9	9			2	4	
Edinburgh 1	223		108	115			71	78			37	37			5	10			72	74			31	31	
Edinburgh 2	56		28	28			20	20			8	8			3	2			16	17			9	9	
Liverpool 1	80		40		40		29		29		11		11		3		3		30		30		7		
Liverpool 2	55	18	18		19	11	11		11	7	7		8				1	14	14		14	4	4		
Liverpool 3	73		25	22	26		18	16	18		7	6	8		1		2		18	18	18		6	4	
London, G O S 1	92	42			50	29			32	13			18	4			3	30			31	8			
London, G O S., 2	68		35	33			29	30			6	3			3	2			23	19			9	12	
London, Q E H 1	105		52		53		33		37		19		16		2		2		31		32		19		
London Q E H., 2	38		13	13	12		11	10	10		2	3	2		1				9	9	9		3	4	
London, S A H	56	28			28	20			21	8			7	2			2	18			19	8			
Manchester	46	25			21	8			10	17			11					21			16	4			
Newcastle	49		25		24		20		18		5		6		2		1		18		18		5		
Sheffield	25	14			11	9			8	5			3	1			1	8			7	5			
Southampton 1	59	27			32	20			21	7			11	1			4	21			21	5			
Southampton 2	44		23	22			12	16			10	6			1				15	16			6	6	
Total	1168	154	416	247	352	97	280	182	230	57	135	65	122	8	23	15	21	112	283	162	241	34	109	70	

TABLE III—NUMBER OF CASES IN EACH TRIAL: INITIAL COMPARABILITY OF TREATMENT GROUPS

Trial	Total no of cases in each treatment group				Source of cases								Average duration of diarrhœa before admission (days)			
					Hospital or other institution				Domiciliary practice							
	A	C	S	R	A	C	S	R	A	C	S	R	A	C	S	R
rmingham 1		37		36		27		19		10		17		3·5		5·1
rmingham 2		12	14			9	12			3	2			7·0	2·8	
dinburgh 1		105	115	}		33	30			104	107		{	4·0	3·7	
dinburgh 2		28	28											3·6	3·1	
verpool 1		40		40		5		11		35		29		3·5		3·3
verpool 2	18	18		19	10	5		9	8	13		10	2·7	3·1		2·6
verpool 3		25	22	26		6	6	7		19	16	19		3·1	4·8	3·3
ondon, G O.S. 1	42			50	19			24	23			26	4·8			6·4
ondon, G O.S., 2		35	33			18	12			17	21			6·0	5·6	
ondon, Q E.H., 1		52		53		11		16		41		37		4·6		4·3
ondon, Q.E.H., 2		13	13	12		2	2	2		11	11	10		5·6	5·6	5·7
ondon, S.A.H	28			*8	10			8	18			20	6·5			4·0
anchester	25			21	4			4	21			17	5·4			4·1
ewcastle		25		*1		5		3		20		31		3·8		3·7
heffield	14			11					14			11	3·4			3·5
uthampton 1	27			32	2			6	25			26	4·6			4·3
uthampton 2		22	22			10	6			12	16			4·1	5·1	

were classified as relapses. An arbitrary distinction was made between relapses and recurrences of diarrhœa later than fourteen days after clinical recovery; these were recorded as separate illnesses.

(f) Additional criteria. At three centres (Birmingham, Liverpool and London, Q E.H.) the following additional criteria were used:

(i) Number of severe cases needing prolongation or renewal of intravenous therapy because oral feeding was not tolerated.

(ii) Number of cases making straightforward progress, with toleration of increasing milk feeds, without setbacks necessitating a return to clear fluids or intravenous therapy

(5) Toxic manifestations attributable to the trial drug

BACTERIOLOGICAL INVESTIGATIONS

Rectal swabs and specimens of fæces were examined at each centre for the presence of salmonella and shigella organisms. In addition at five of the centres (Birmingham Edinburgh, Liverpool London, S.A.H and Southampton) examinations were made for *Escherichia coli* O 111 and *B coli O 55* These specific serological types have been found in many countries in recent years in association with infantile diarrhœa and vomiting and some workers have reported their isolation from a larger proportion of severe cases than of mild ones (Holzel et al 1949 Alexander et al 1952) At each of the five centres concerned the *B coli* O 111 and *B coli* O 55 strains isolated from cases at entry to the trial were examined by biochemical and serological methods, the O group being identified by tube agglutination tests.

Clinical Findings

Altogether 1168 cases of infantile diarrhœa and vomiting (789 mild, 379 severe) were included in the analysis of the results of these cases 154 were aureomycin-treated, 415 chloramphenicol treated, 247 sulphadiazine-treated, and 352 controls. The response to treatment of individual cases was assessed solely by their clinical progress

The results in different treatment groups were compared in two stages

(1) The *first stage* was to consider each trial separately The investigation had been so designed as to ensure the allocation of cases of similar age and severity to different treatment groups. The concurrent series in each trial were analysed to verify that the age and severity distributions of the cases were similar and to demonstrate by the other criteria chosen, that the treatment groups were initially comparable. They were further examined to ascertain whether the cases in each group had received similar treatment apart from the administration of the trial drug The treatment groups were next compared as regards the criteria of clinical progress previously listed.

(2) The *second stage* was to bring together the findings obtained at different centres, by collecting the results of all trials in which there were two similar treatment groups. Variations in treatment between different centres were examined The results at centres found to show important variations were analysed separately The results at the remaining centres were combined

The following treatment groups were then compared:

A R, aureomycin treated and concurrent controls.
C R chloramphenicol treated and concurrent controls
C-S chloramphenicol treated and concurrent sulphadiazine treated.

STAGE 1 RESULTS OF SEPARATE TRIALS

Initial Comparability of Treatment Groups

Table II shows the number of cases included in each trial and the distribution of the cases according to their treatment group and to severity of illness and age on entry to the investigation.

Table III shows, for each of the concurrent series the sources of the cases and the average duration of diarrhœa before entry to the investigation. In both these characteristics the different treatment groups as shown in the following summary of table III were similar enough to justify comparisons between them of subsequent clinical progress

Treatment groups	*Percentage of cases from domiciliary practice*		*Average duration of diarrhœa before entry to trial*
A R	A 71 %	R 68 %	A 4·9 days, R 4·6 days
C-R	C 71 %	R 68 %	C 3·8 days, R 4·0 days
C-S	C 68 %	S 70 %	C 4·3 days, S 4·2 days

Variations in Treatment

Details of routine treatment varied at different centres, but each centre aimed to apply its usual methods to all cases irrespective of the treatment group to which they were allocated Possible bias in this respect was obviated at two centres (Edinburgh 2nd trial and London S.A.H.) where trials were conducted blind —i.e., without the physicians knowing which patients were receiving the trial drug

All patients in the treatment groups A C and S were given the respective drug according to the agreed dosage. Patients in the control group (R) were normally given no antibiotic or chemotherapeutic agent by mouth during the first week of treatment At one centre (London S.A H) sulphadiazine was given by mouth in all severe cases, irrespective of the treatment group At another centre (London, Q.E H) penicillin was given intramuscularly in all severe cases as a routine prophylactic measure during intravenous therapy

Infants found to have, either at the time of their entry to the investigation or during the subsequent course of their illness, a parenteral infection considered to need

TABLE IV—CLINICAL PROGRESS OF CASES IN EACH OF THE TRIALS

Trial	Total no of cases				No of deaths				No of survivors				Average duration of diarrhœa after entry (days)				Average time to clinical recovery (days)				No of mild cases which became severe				No of cases which relapsed			
	A	C	S	R	A	C	S	R	A	C	S	R	A	C	S	R	A	C	S	R	A	C	S	R	A	C	S	R
Birmingham 1		37		36		3		1		34		35		5 7		8 0		10 6		13 1		1		4		3		1
Birmingham 2		12	14				1			12	13			12 9	6 5			16 3	11 5			1	1					
Edinburgh 1		108	115			5	2			103	113			5 4	4 8			15 4	13 8			5	5			6	4	
Edinburgh 2		28	28							28	28			3 7	3 2			14 8	14 7							2		
Liverpool 1		40		40				4		40		36		5 2		10 2		11 1		17 7				4				
Liverpool 2	18	18		19				1	18	18		18	7 4	5 2		10 6	12 7	11 3		18 7	2	1		4	2			
Liverpool 3		25	22	26		1	1			24	21	26		7 9	6 0	10 9		11 0	8 8	13 9		2	1	7		1	1	
London, G O S , 1	42			50	1			3	41			47	14 2			17 2	17 6			20 4	1			14	3			1
London, G O S , 2		35	33							35	33			14 6	9 5			18 5	12 5			2				3	4	
London, Q E H , 1		52		53						52		53		5 1		8 3		8 0		12 0				6		6		1
London, Q E H 2		13	13	12						13	13	12		4 5	4 9	7 2		6 3	6 5	9 2			1	1			3	1
London S.A H	28			28	1				27			28	4 9			6 0	13 8			12 8	1			5	7			[illegible]
Manchester	25			21	1			2	24			19	7 4			8 9	14 2			14 5	1			2				
Newcastle		25		24						25		24		9 1		6 8		13 6		13 9				2		1		[illegible]
Sheffield	14			11	2			2	12			9	6 9			5 7	12 2			14 1								
Southampton 1	27			32	1			1	26			31	6 4			4 6	10 9			9 3	1							1
Southampton 2		22	22							22	22			7 0	9 1			10 0	12 0				3			2	3	

specific treatment were usually given penicillin intramuscularly Sulphonamides or antibiotics other than the drug appropriate to the treatment group were given by mouth to some patients whose progress was considered to be unsatisfactory and to some patients for the treatment of parenteral infections Details of such additional chemotherapy are recorded in the second stage of the analysis of the results

Clinical Progress

Table IV gives the results obtained in each of the trials It shows the number of cases included in the investigation at each centre and their clinical progress as regards the criteria chosen. Durations of diarrhœa and times to clinical recovery have been expressed as averages for each treatment group The relation of clinical progress to treatment group is seen to follow a general trend from more rapid recovery in the sulphadiazine treated and chloramphenicol-treated groups to less rapid recovery in the aureomycin-treated and control groups The statistical significance of the observed differences is dealt with in the second stage of the analysis

STAGE 2 COMPARISON OF TREATMENT GROUPS

Aureomycin treated and Concurrent Control Groups

The numbers for comparison from the six centres concerned (Liverpool 2, London, G O S 1, London, S A H , Manchester, Sheffield, and Southampton 1), were 154 cases in the aureomycin treated group and 161 cases in the control group

The method of the trial at London, S.A H differed from that at the other centres in several important respects the trial was, throughout, conducted " blind ", cases within each age and severity group were allocated at random to treatment groups, all the control patients were given by mouth an inert yellow powder indistinguishable in appearance from aureomycin, and all severe cases were treated with sulphadiazine by mouth, irrespective of treatment group The results obtained at this centre have therefore been analysed separately

Important variations also were recorded at London, G O S , where sulphonamide derivatives were given by mouth to 7 of the 42 patients in the aureomycin-treated group and to 27 of the 50 controls Additional antibiotic therapy given to controls comprised the following, either chloramphenicol or aureomycin by mouth to 13 infants whose clinical condition was not improving under routine treatment, penicillin parenterally in 14 cases, and streptomycin parenterally in 8 cases The variations recorded were sufficiently large to necessitate separate analysis of the results obtained at this centre

At the other centres using aureomycin additional chemotherapy was given in only a small proportion of cases, mainly in the control group

Table V shows a comparison of the aureomycin treated and concurrent control groups At London, G O S the proportion of mild cases becoming severe was significantly higher in the control group (χ^2 = 11 24 n = 1 P<0 001) This difference, which was supported by the results at London, S A H , was the only statistically significant difference between the two treatment groups No statistically significant difference was demonstrated, at any of the centres, in the average duration of diarrhœa after entry to the trial or in the average time to clinical recovery The number of cases relapsing after clinical recovery was slightly higher in the aureomycin treated group

Chloramphenicol-treated and Concurrent Control Groups

The numbers for comparison from the four centres concerned (Birmingham 1, Liverpool 1, 2, and 3, London, Q E H , 1 and 2, and Newcastle) were 210 cases in the chloramphenicol-treated group and 210 cases in the control group The principles of routine treatment were similar at all four centres At Birmingham 4

TABLE V—COMPARISON OF AUREOMYCIN TREATED (A) GROUPS AND CONCURRENT CONTROL (R) GROUPS

—	Centre	Mild cases		Severe cases		Total	
		A	R	A	R	A	R
Total no of cases	London, G O S	29	32	13	18	42	50
	London, S A H	20	21	8	7	28	[illegible]
	Other centres	48	50	36	33	84	83
No of deaths	London, G O S			1	3	1	3
	London S A H			1		1	
	Other centres	2	2	2	4	4	6
No of survivors	London, G O.S.	29	32	12	15	41	47
	London, S A.H	20	21	7	7	27	28
	Other centres	46	48	34	29	80	[illegible]
Average duration of diarrhœa after entry to trial (days)	London G O S	13 5	17 1	16 0	17 5	14 9	[illegible]
	London S.A H.	4 6	5 0	6 2	7 4	4 9	[illegible]
	Other centres	6 9	7 1	7 1	7 3	7·0	[illegible]
Average time to clinical recovery (days)	London, G O.S	16 9	20 3	19 3	20·5	17·6	[illegible]
	London S A.H	14 5	13 3	11 9	11 1	13 5	[illegible]
	Other centres	11 3	12 7	14 1	14 4	12 5	[illegible]
No of mild cases which became severe	London, G O S	1	14				
	London S A.H	1	5				
	Other centres	4	6				
No of cases which relapsed	London G O S	2	1	1		3	1
	London, S A.H	4	6	3	1	7	1
	Other centres	2			1	2	1

patients all in the control group, were given sulphonamides by mouth because of unsatisfactory progress At Liverpool 3 patients in the chloramphenicol treated group were later given either penicillin or streptomycin intramuscularly for the treatment of parenteral infections, in the control group some patients were given penicillin intramuscularly and 2 patients whose condition was deteriorating were given chloramphenicol by mouth after the end of the first week of treatment At London Q E H., penicillin was given intramuscularly to patients in both groups for the treatment of parenteral infections, in the control group 8 patients, whose conditions were deteriorating, were given chloramphenicol by mouth after intervals ranging from six to fourteen days from the start of treatment. At Newcastle 2 patients in the chloramphenicol treated group were given penicillin intramuscularly for parenteral infections and in the control group most of the patients were given penicillin intramuscularly, 6 were given sulphadimidine by mouth, 4 were given streptomycin, and 2 aureomycin and 2 whose condition was deteriorating were given chloramphenicol by mouth after the end of the first week of treatment. The recorded variations in treatment were proportionately greater at Newcastle than at the other centres using chloramphenicol but the numbers involved were comparatively small. The results at all four centres have therefore been combined in the second stage of the analysis.

TABLE VI—COMPARISON OF CHLORAMPHENICOL TREATED (C) GROUPS AND CONCURRENT CONTROL (R) GROUPS

—	Mild cases		Severe cases		All cases	
	C	R	C	R	C	R
Total no. of cases	138	138	72	72	210	210
No. of deaths	1	2	3	4	4	6
No. of survivors	137	136	69	68	206	204
Average duration of diarrhœa after entry (days)	5·6	8·3	6·7	10·0	6·0	8·9
Average time to clinical recovery (days)	9·6	13·1	11·5	15·6	10·3	14·0
No. of mild cases which became severe	4	23				
No. of cases which relapsed	4	5	6	2	10	7

Total no. of cases	118	120	67	66	Additional criteria used at three of the centres
No. of severe cases which needed prolonged intravenous therapy			3	28	
No. of cases which made straightforward progress	110	79	64	37	

Table VI shows a comparison of the chloramphenicol treated and concurrent control groups The average duration of illness after entry to the trial was less in the chloramphenicol treated group than in the control group. Statistically significant differences in favour of the chloramphenicol treated group were demonstrated as regards the average duration of diarrhœa ($t = 4·98$, $n = 408$, $P < 0·001$) the average time to clinical recovery ($t = 4·66$ $n = 408$, $P < 0·001$) and the numbers of mild cases becoming severe ($\chi^2 = 20·36$, $n = 1$, $P < 0·001$) The relative improvement in progress in the chloramphenicol-treated group was of the same order in both mild and severe cases. The number of cases relapsing after clinical recovery was small but was higher in the chloramphenicol treated group

Chloramphenicol treated and Concurrent Sulphadiazine treated Groups

The numbers for comparison from the six centres concerned (Birmingham 2, Edinburgh 1 and 2, Liverpool 3, London, G O.S. 2, London, Q E H, 2, and Southampton 2) were 243 cases in the chloramphenicol treated group and 247 cases in the sulphadiazine treated group The principles of routine treatment were similar at all six centres Penicillin was given intramuscularly for the treatment of parenteral infections to some patients in each of the treatment groups. Apart from this additional antibiotic or chemotherapeutic treatment was rarely given. The variations recorded were not so numerous as to invalidate comparison of the two treatment groups At two of the centres (Liverpool 3 and London, Q E H., 2) concurrent series of control cases allowed a comparison of three treatment groups (C S, and R)

TABLE VII—COMPARISON OF CHLORAMPHENICOL TREATED (C) GROUPS AND CONCURRENT SULPHADIAZINE-TREATED (S) GROUPS

—	Mild cases		Severe cases		All cases	
	C	S	C	S	C	S
Total no of cases	171	182	72	65	243	247
No. of deaths	2	0	1	4	6	4
No of survivors	169	182	68	61	237	243
Average duration of diarrhœa (days)	7·1	5·7	7·8	6·3	7·3	5·8
Average time to clinical recovery (days)	13·5	12·0	16·5	14·5	14·1	12·6
Number of mild cases which became severe	10	11				
Number of cases which relapsed	7	13	7	2	14	15

Table VII shows a comparison of the chloramphenicol treated and concurrent sulphadiazine-treated groups. The average duration of illness after entry to the trial was less in the sulphadiazine-treated group than in the chloramphenicol treated group Statistically significant differences in favour of the sulphadiazine treated group were demonstrated as regards the average duration of diarrhœa ($t = 2·30$, $n = 478$ $0·01 < P < 0·02$) and the average time to clinical recovery ($t = 2·50$ $n = 478$, $0·01 < P < 0·02$) The relative improvement in progress in the sulphadiazine-treated group was of the same order in both mild and severe cases. There was no significant difference between the two treatment groups in the proportion of mild cases becoming severe.

A direct comparison of sulphadiazine-treated and control groups was made at two centres only (Liverpool 3 and London, Q.E H, 2) In concurrent series at these centres 38 cases were allocated to the chloramphenicol treated group 35 cases to the sulphadiazine treated group, and 38 cases to the control group Significant differences were demonstrated between the sulphadiazine-treated and control groups as regards the average duration of diarrhœa after entry to the investigation ($t = 2·40$ $n = 70$ $0·01 < P < 0·02$) and the average time to clinical recovery ($t = 2·77$ $n = 70$ $P < 0·01$) The differences between the chloramphenicol treated and control groups were statistically not quite significant it is reasonable

TABLE VIII—DISTRIBUTION ON ENTRY TO THE TRIALS OF *E coli* O 111 AND *E coli* O 55 POSITIVE AND NEGATIVE CASES RESULTS FROM THE FIVE CENTRES CONCERNED

Trial	No. of cases *E. coli* O 111 positive				No. of cases *E coli* O 55 positive				No of cases *E. coli* O 111/O 55 negative				Total no. of cases			
	A	C	S	R	A	C	S	R	A	C	S	R	A	C	S	R
Birmingham 1		11		6		21		15		5		15		37		36
Birmingham 2			3							12	11			12	14	
Edinburgh 1		20	19			17	17			64	69			101	105	
Edinburgh 2		4	5			9	8			16	14			29	27	
Liverpool 1		14		15		7		5		19		20		40		40
Liverpool 2	11	10		11					7	8		8	18	18		19
Liverpool 3		11	10	8						14	12	12		25	22	20
London, S.A H	5			4	2			2	21			22	28			28
Southampton 1	1			2				1	26			29	27			32
Southampton 2		1				4	3			17	19			22	22	

to assume that this was due to the small numbers of cases, because the actual differences observed were of the same order as those observed in other C-R series

NUMBER OF DEATHS

The total number of deaths was 33, giving an over all fatality rate of 2 8% The numbers of deaths in each treatment group, with the corresponding fatality-rates, were aureomycin-treated 6 (3 9%), chloramphenicol treated 9 (2 2%), sulphadiazine-treated 4 (1 6%), controls 14 (4 0%)

TOXIC MANIFESTATIONS ATTRIBUTABLE TO TRIAL DRUGS

In a small proportion of cases skin eruptions were observed that were attributable to possible toxic effects of the drug under trial In the chloramphenicol-treated group 14 infants developed rashes, 6 of these were eczematous in appearance and associated with blood eosinophilia, 2 cases of exfoliative dermatitis were recorded In the aureomycin-treated group 3 infants developed erythema of the hands and feet, and 2 others developed induration of the hands In the sulphadiazine treated group skin rashes were reported in 3 cases

Bacteriological Findings

Infants admitted to the investigation and found to have either salmonella or shigella infection were excluded from the analysis of the clinical results Of the remaining 1168 cases 745 were treated at the five centres where examinations were made for *E coli* O 111 and *E coli* O 55

Table VIII shows the results obtained from examination of rectal swabs, or of specimens of fæces, taken from these infants at the time of their entry to the investigation or, in some cases, on the day after their entry. The results refer to 727 patients from whom specimens were collected before treatment was begun with aureomycin, chloramphenicol, or sulphadiazine 18 cases were excluded because relevant specimens were either not obtained or not examined

It is seen from table VIII that at four of the five centres, among a total of 628 cases, these specific *E coli* types were found to be almost equally distributed between the respective treatment groups of cases in each trial This finding afforded additional evidence, independent of the clinical observations, of the initial comparability of the treatment groups at these four centres The observed differences between the groups, as regards clinical response to treatment, could not therefore be attributed to the preponderance, in any one group, of cases from which these *E coli* types were isolated at the time of entry to the trial At the fifth centre (Birmingham), for no known reason, *E coli* O 111 and *E coli* O 55 were isolated from chloramphenicol-treated patients in higher proportion than from the concurrent controls

Separate reports are in preparation at two centres (Edinburgh and Liverpool) regarding the relation of the bacteriological findings to the clinical progress of their cases

Discussion

It has long been recognised that non specific infantile diarrhœa and vomiting is, in many instances, a manifestation of some acute infection Because the identity of the infective agent, or agents, concerned has not yet been established, treatment of the disease with chemotherapeutic or antibiotic drugs has lacked an experimental basis Nevertheless in the past ten to fifteen years most of the sulphonamides and the newer antibiotics have been tried empirically, and their effects on the course of the illness judged by clinical observations During the same period the prognosis of infantile [illegible] and vomiting has greatly improved, a change contemporaneous with the adoption of more effective measures for the treatment of dehydration Results attributed to particular drugs need therefore to be considered in relation to improvements in current methods of routine treatment

Many of the published results are difficult to assess Some workers have treated cases with chemotherapeutic or antibiotic agents and have reported their results without reference to concurrent control cases treated by routine methods Others have described controlled investigations of cases in numbers too small to have established statistically significant differences between the treatment groups Well controlled trials with adequate numbers of cases have been relatively uncommon In Great Britain the therapeutic use of streptomycin has been tested critically by several groups of workers (Holzel et al 1949, Lowdon and McNeill 1951, Young et al 1951, Alexander et al 1952), who failed to substantiate the claims made for this drug by previous investigators

Various sulphonamides have been used for the treatment of infantile diarrhœa and vomiting Favourable results have been reported with sulphathiazole (Taylor 1941), succinylsulphathiazole (Twyman and Horton 1943), sulphaguanidine (Henderson 1943), and sulphadiazine (Kirsch and Nieckau 1943, Tudor 1943), A controlled investigation of sulphadiazine was made by Klose (1947), who found that the drug did not appear to have any effect on the course of the disease Some workers have continued to use sulphonamides for the treatment of associated parenteral infections, and a few have considered that these drugs may exert a favourable influence even in the absence of signs of parenteral infection, though opinions on this matter have been divided (see Hinden 1948)

Good results have also been reported with the use of chloramphenicol (Rogers et al 1949, Clément et al 1950, Smellie 1950, Piette and Vézina 1951) and of aureomycin (Magnusson et al 1950, Laurell et al. 1951, Sacrez et al 1951, Chedid et al 1951) In a controlled investigation of both of these antibiotics Shanks (1951) found no significant difference between either of the two treated series and the controls, but it is noteworthy that the controls were given penicillin and/or sulphonamides as indicated, on the assumption that neither of the two latter drugs could be regarded as in any way specifically effective in the treatment of infantile diarrhœa

The results of the present trials showed that the groups of patients treated with either sulphadiazine or chloramphenicol progressed more favourably than the group given routine treatment only, and that benefit to a more limited extent might also be attributed in some cases to treatment with aureomycin Analysis of the findings was complicated by the introduction of sulphadiazine into trials designed originally to investigate the effects of either aureomycin or chloramphenicol. Some of the early results suggested that sulphadiazine was at least as effective in treatment as chloramphenicol This necessitated the separate consideration of those trials in which sulphadiazine was extensively used in the treatment of the control cases As evidence of the value of sulphadiazine accumulated, further trials were deliberately designed to compare the effects of sulphadiazine with those of chloramphenicol

In the trials of aureomycin no statistically significant difference was demonstrated between the aureomycin-treated and control groups in their average durations of diarrhœa or average times to clinical recovery At two of the centres concerned (London, G O S, and London, S A H) the interpretation of this finding was rendered uncertain by reason of the use at these centres of sulphadiazine in the treatment of control cases At the same two centres it was found that the number of mild cases becoming severe was significantly less in the aureomycin treated group, a result unlikely to have been influenced by the use of sulphonamides, since chemotherapeutic agents were seldom given in mild cases in the control group unless the clinical condition had already begun to deteriorate. At the other centres using aureomycin no significant difference between the aureomycin treated and control groups was shown as regards any of the chosen criteria of clinical progress in spite of the fact that only a few of the controls were treated with sulphonamides. The evidence obtained therefore suggests that aureomycin prevented deterioration in some of the mild cases at two of the centres but no other beneficial effect of the drug was detected.

In contrast, the results obtained in the trials of chloramphenicol showed that this drug was effective in shortening the duration of diarrhœa and in hastening clinical recovery It was also found to be effective in preventing mild cases from becoming severe and in promoting straightforward progress in both mild and severe cases Similar routine treatment was given to all the cases, both chloramphenicol treated and controls and relatively few of the controls were treated with any chemotherapeutic or antibiotic agent by mouth Occasionally controls were given chloramphenicol when at the end of at least five days routine treatment their clinical condition was causing anxiety The numbers involved were small, and the significance of the differences between the two treatment groups was not obscured by this additional therapy

The trials designed to compare the effects of chloramphenicol with those of sulphadiazine arose as a result of the findings at one centre (Edinburgh) where sulphadiazine was given by mouth as part of the routine treatment. Preliminary results at this centre suggested that sulphadiazine might prove to be at least as effective as chloramphenicol. Subsequent trials supported this conclusion In the final analysis significant differences in favour of the sulphadiazine-treated group were found as regards the average duration of diarrhœa and time to clinical recovery There was no significant difference between the two groups in the proportion of mild cases becoming severe At two centres (Liverpool and London, Q E H) where the progress of concurrent control groups was also studied, the results confirmed the efficacy of sulphadiazine compared with routine, treatment.

In assessing the results of the investigation as a whole it should be emphasised that all the trials were made against a background of highly effective supportive treatment. The fatality rate was 2 8% of the total cases and, even in the control group was not higher than 4% The number of deaths in the control group may have been influenced by the use of chemotherapeutic or antibiotic agents which were given to some infants, whose clinical condition was deteriorating, to improve their chances of recovery For this reason the fatality rate was considered an unreliable criterion for the comparison of trial and control groups. The differences between the fatality rates in the various treatment groups, though not large enough to be statistically significant, were consistent, however with the differences observed as regards the other criteria of clinical progress.

More than half the controls made straightforward progress to recovery without chemotherapeutic or antibiotic treatment. Nevertheless the proportion of mild cases becoming severe was significantly greater in the control group (14%) than in the aureomycin treated (4%) chloramphenicol treated (3%) or sulphadiazine-treated (4%) groups. This finding suggests an important use for these drugs in the prevention of clinical deterioration of mild cases not responding initially to routine methods of treatment. Moreover the administration of sulphadiazine or of chloramphenicol but not of aureomycin, was shown to reduce the average duration of illness in both mild and severe cases.

Selection of the most appropriate drug for the treatment of individual cases of infantile diarrhœa and vomiting may become possible when more is known of the ætiology of the disease. The results of the present investigation indicate sulphadiazine and chloramphenicol as the drugs of choice, with the balance of evidence in favour of sulphadiazine, and their oral administration may be considered as a valuable addition to established methods of treatment It should be realised, however, that adequate supportive therapy still remains of paramount importance and that treatment with either of these drugs is not devoid of the risk of toxic manifestations attributable to their use.

Summary

Controlled trials of aureomycin, chloramphenicol, and sulphadiazine in the treatment of infantile diarrhœa and vomiting were made at ten separate centres in Great Britain during 1950–52.

The trial drugs were administered by mouth in doses of respectively 75 mg, 75 mg., and 125 mg per lb body weight a day for seven days

A total of 1168 cases (789 mild, 379 severe) was included in the analysis of the results. Infants found to have either salmonella or shigella infections were excluded from this analysis.

The numbers in the different treatment groups were 154 aureomycin treated 415 chloramphenicol treated 247 sulphadiazine treated and 352 controls The mean fatality rate was 2 8%

Clinical progress after the start of treatment was assessed on the following criteria average duration of diarrhœa average time to full clinical recovery and proportion of mild cases which became severe.

The aureomycin treated group progressed more favourably than the controls as regards the proportion of mild cases which became severe but not as regards the two other criteria

The chloramphenicol treated and sulphadiazine-treated groups progressed more favourably than the controls as regards all three criteria. The progress of the sulphadiazine-treated group was significantly better than that of any other treatment group

The use of aureomycin, chloramphenicol, or sulphadiazine as a therapeutic measure additional to established routine methods of treatment is discussed.

The Working Party desires to express its thanks for facilities afforded by hospital and other authorities at the centres concerned; and for the assistance of those members of the medical nursing and technical staffs who coöperated in this investigation.

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GASTRIC ASPIRATION IN HÆMATEMESIS

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The early recognition of recurrent hæmorrhage and the accurate identification of the site of bleeding in hæmatemesis and melæna are of great clinical importance but are also beset with difficulties Kinsella (1950) reported favourably on the use of an indwelling tube for the recognition of recurrent hæmorrhage There is a real need for a safe bedside method that would yield reliable diagnostic and prognostic information

It was thought that in the acute stages of gastroduodenal hæmorrhage some abnormality of gastric secretion of diagnostic value might be present For this reason 24 hour gastric analysis (James and Pickering 1949) previously used in the study of peptic ulcer and achlorhydria (Watkinson 1951, Watkinson and James 1951) has been applied to the problem We report here the results of twenty four-hour gastric analysis in 105 consecutive and unselected patients admitted, as emergencies, with hæmatemesis or melæna to the medical wards of the General Infirmary at Leeds and St James's Hospital, Leeds, in the last year

TABLE I—CLINICAL MATERIAL STUDIED

Diagnosis	No of cases	Diagnostic criteria				
		Operation	Radiography		Gastroscopy	Necropsy
			Positive	Negative		
Chronic G U	17	6	9		5	
Chronic D U	35	6	32			1
Acute ulcer	42	5	2	31	13	2
Postoperative bleeding	7	4	2		5	
Hiatus hernia	4		4			

In many patients the investigations were duplicated.

Procedure

The modern régime for the treatment of hæmatemesis was followed, with early and liberal feeding as recommended by Meulengracht (1935) and modified in this country by Witts (1937), together with the generous use of blood by drip transfusion A Ryle's tube was passed shortly after admission and, where feasible, the position of the tip of the tube was assessed radiologically and adjusted to the angulus X ray control was impracticable in the acutely ill patients and this is a potential source of error in this study 5–10 ml of stomach contents was aspirated hourly by day and by night, and the pH of these unfiltered samples was estimated with a sealed glass electrode The presence of recent or old blood-staining in the aspirated specimens was recorded on a chart devised for the purpose, on which measurements of pulse rate and blood pressure were also plotted, together with the amounts of transfused blood and episodes of further hæmorrhage In this way a continuous and sequential record of progress was readily available at the bedside, and proved of great value in the hour-to-hour management of each patient No evidence was obtained to suggest that the presence of an indwelling tube stimulated recurrence of bleeding or favoured its continuance or that the mortality rate was adversely affected The dangers of this procedure appear to be largely theoretical, and in our opinion anxiety on this score is unwarranted The tube was left in situ for periods averaging between forty-eight and seventy two hours, aspirations being continued for at least twelve hours after bleeding had ceased The patients tolerated the procedure well, the small interference necessary to obtain the gastric samples neither disturbing sleep nor impairing appetite

Confinement of the patient to bed at strict rest was enforced for at least three weeks when barium examination of the stomach and duodenum was undertaken. Some patients were gastroscoped in the first week when it was thought that this would prove helpful to diagnosis. In the remainder verification was obtained either at operation or at necropsy

Clinical Material

Many workers have emphasised the difficulty of identifying the site of bleeding in hæmatemesis, since in the acute stages there is no certain method of diagnosis save operation, and the final conclusion must be reached in retrospect Even at necropsy it may be impossible to decide the source of bleeding, particularly if multiple lesions exist Only by the careful integration of early gastroscopy and comprehensive radiological control can results comparable to those achieved by Avery Jones (1952) be obtained, and we have adopted a method of classification similar to that used by him

Chronic Gastric Ulcer

Of the 17 patients in this group the ulcer was shown at operation in 6, by radiological examination in 9, and at gastroscopy in 4, the investigations being duplicated in 3 patients All the ulcers were reckoned benign Associated lesions included 1 patient with hiatus hernia, 1 with pyloric stenosis, and 1 with duodenal ulcer

Chronic Duodenal Ulcer

Of the 35 patients so classified the ulcer was demonstrated at operation in 6, radiologically in 32, and at necropsy in 1 Associated lesions were pyloric stenosis in 1 patient, hiatus hernia in 2, and carcinomatosis and cardiac infarction in the fatal case

Acute Ulcer

The following criteria have determined this classification in 42 patients

Gastroscopic confirmation —Definite evidence of acute ulcer was obtained in 13 patients by gastroscopy done within a week of admission

Operative and necropsy verification —Acute ulceration was confirmed at operation in 5 patients and at necropsy in 1

Positive radiological evidence —The presence of an ulcer crater without deformity of the duodenal cap enabled a confident radiological diagnosis of acute duodenal ulcer to be made in 2 patients

Negative radiological findings —In 31 patients a negative barium meal examination, done three weeks after hæmorrhage had ceased, allowed the presumptive diagnosis of acute peptic ulcer

TABLE II—AGE AND SEX DISTRIBUTION OF PATIENTS STUDIED

Diagnosis	Sex	Age (yr)							Tot
		0–20	21–30	31–40	41–50	51–60	61–70	70+	
Chronic G U	M			3	5	1	2	1	13
	F				2	1		2	5
Chronic D U	M	1	1	6	8	10	5	1	31
	F			1	1		1	1	4
Acute ulcer	M	1	4	8	3	6	1	2	25
	F	1	1	2	3	5	4	1	17
Postoperative bleeding	M				3	4			7
	F								
Hiatus hernia	M				1		1	1	3
	F						1		1
Total		3	6	10	20	27	15	9	10

Postoperative Group

Of the 7 patients in this group gastro-enterostomy had been performed for chronic duodenal ulcer in 4 and for gastric carcinoma in 1 3 patients had previously been ubmitted to gastrectomy for duodenal ulceration Operation showed chronic duodenal ulcer as the site of bleeding in 2 patients and anastomotic ulcer in 2.

Œsophageal Hiatus Hernia

4 patients were shown to have hiatus hernia and reflux œsophagitis, hæmorrhage presumably originating in that site

The *diagnostic criteria* are summarised in table I

The *age and sex distribution* of the patients studied are summarised in table II and are similar to those of the largest reported series. The usual male preponderance was found in the chronic ulcer group acute peptic ulcer being relatively more common in women (Avery Jones 1952)

The *length of a history* of preceding dyspepsia supported the eventual diagnosis (fig 1); 36 of the 52 patients with chronic ulcers had had dyspepsia for more than five years, and 13 between one and three years Of the 42 patients in the acute ulcer group 18 gave histories of less than a week, 4 between one or two weeks and 8 between two and four weeks.

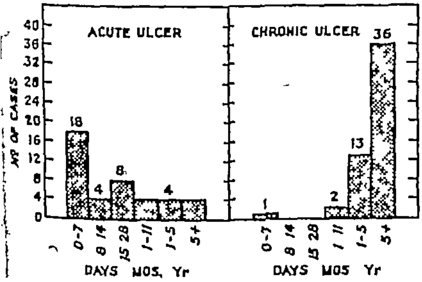


Fig. 1—Relation of length of history to type of ulcer finally diagnosed. Of 52 patients with chronic ulcer 36 patients had histories of dyspepsia exceeding 5 years and 13 of 1–5 years; whereas of 42 patients with acute ulcer 18 had histories of less than a week, 4 of 1–2 weeks, and 8 of 2–4 weeks.

Value of Gastric Aspiration in Management of Patient

SIGNIFICANCE OF BLOODSTAINING

The bedside observation of bloodstaining in the aspirated specimens was found of great value in the treatment of individual patients, because warning of further hæmorrhage might thus be obtained before other clinical criteria indicated it occasionally information about the site of the ulcer was provided. The finding of fresh blood in the hourly specimens is to be expected in the early stages after gastroduodenal hæmorrhage, and the usual course of events (fig 2) is for this staining to diminish in intensity and to appear older until the samples are finally returned clear Bloodstaining was usual in patients with chronic gastric ulcer (14 of 17 cases) was less frequently observed in acute ulcer (23 of 42) and was least common in chronic duodenal ulcer (16 of 35)

Evidence about the site of the ulcer was obtained in 7 patients admitted with hæmatemesis. In these patients, though bleeding continued with the passage of frequent melæna stools, the gastric samples became rapidly clear indicating that the site of hæmorrhage lay distal to the stomach. All these patients, as anticipated, had duodenal lesions, and 3 required surgery for their eventual control. Fig 3 illustrates the findings in 1 patient whose continued melæna necessitated the transfusion of 10 pints of blood in the first two days; the gastric aspirations showed old blood by the third hour and later cleared completely The association of clear specimens with evidence of continued bleeding usually indicates that the source of bleeding is beyond the pylorus

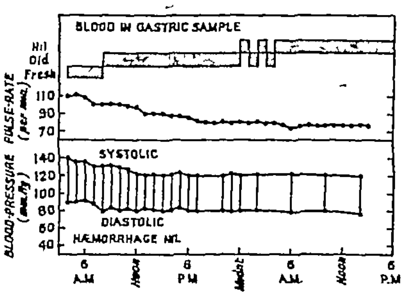


Fig. 2—Results of hourly gastric aspiration in a patient with a gastric ulcer After initial fresh bloodstaining samples contain old blood and become finally clear indicating cessation of bleeding.

The imminence of recurrent hæmorrhage has been anticipated, often by many hours, by the reappearance of fresh blood in the aspirated specimens, before other criteria have indicated relapse. The patient whose chart is shown in fig 4 was bleeding from a chronic gastric ulcer After twice vomiting blood on the first day he appeared to improve with the transfusion of 3 pints of blood Although there was no further evidence of hæmorrhage in the next three days, blood was consistently present in the aspirated specimens, antedating by many hours the hæmatemesis on the fifth day Early recognition of recurrent hæmorrhage was similarly forthcoming in 26 patients, proving most useful in those with acute and chronic gastric ulcers and of least value in patients with duodenal lesions.

SIGNIFICANCE OF INTRAGASTRIC pH

The method of twenty four hour gastric analysis aims at studying changes in gastric acidity on a normal diet and has yielded interesting results in the study of peptic ulcer and achlorhydria (James and Pickering 1949 Watkinson 1951 Watkinson and James 1951) Though

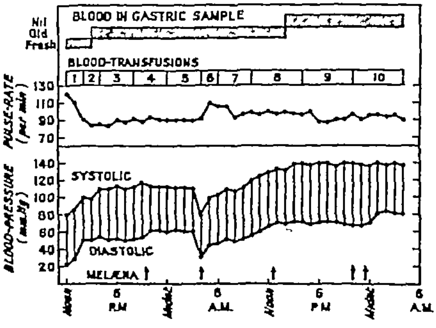


Fig. 3—A patient with a bleeding duodenal ulcer studied by hourly gastric aspiration. Although bleeding was obviously continuing (judged by pulse-rate, melæna, and necessity for continued transfusion) gastric samples became rapidly clear indicating that source of hæmorrhage was distal to stomach.

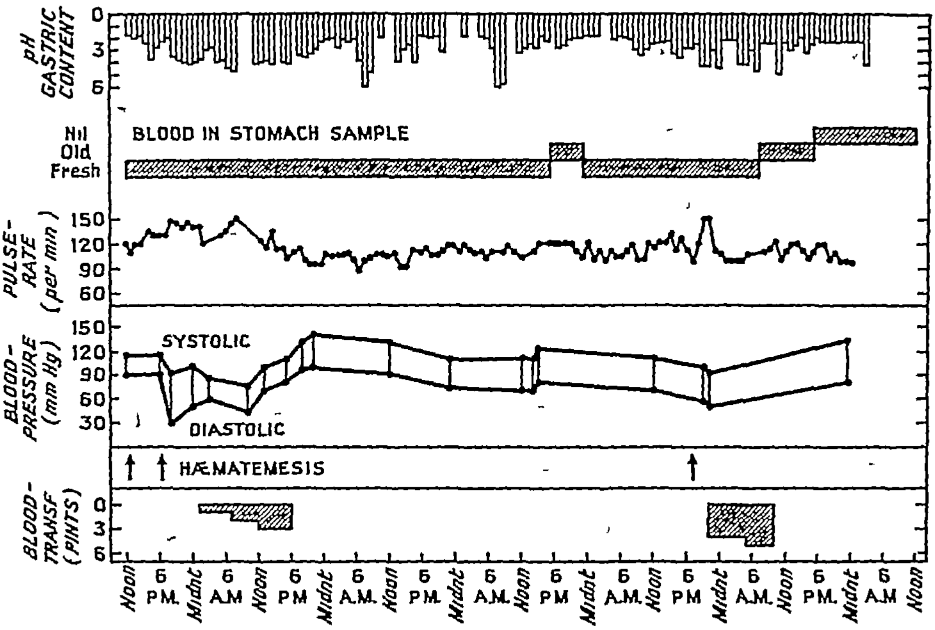


Fig 4—Hourly gastric aspiration in a patient bleeding from a chronic gastric ulcer, after 2 hæmatemeses on the first day clinical criteria suggested that bleeding had ceased, but copious amounts of fresh blood were aspirated in the next 3 days and antedated by many hours the third hæmatemesis on the fifth day

normal people show considerable variability in nocturnal pH, acid values are rarely more alkaline than pH 4 5 In patients with duodenal ulceration a high night acidity is usual, whereas about half the patients with gastric ulcer show steep nocturnal falls in acidity approximating to alkaline levels

In this investigation the changes in gastric acidity were estimated immediately after gastroduodenal hæmorrhage in an attempt to obtain diagnostic information. Three types of abnormal secretion pattern were recognised

(1) *Nocturnal neutralisation*—In patients of this type nocturnal reductions in acidity approximating to alkaline levels were observed and pH values exceeding 5 5 were obtained 2 examples are shown in fig 5

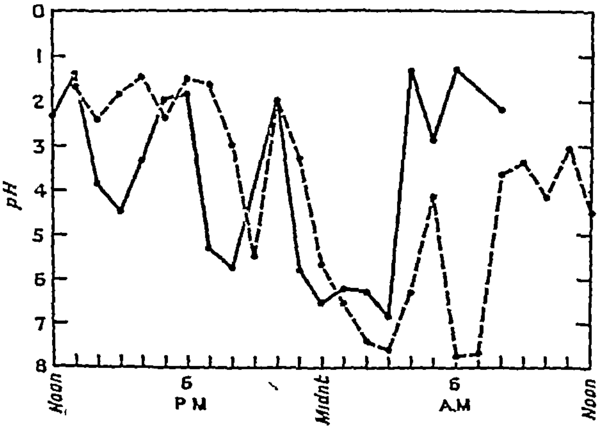
(2) *High nocturnal acidity*—In these patients the night acidity is abnormally high, lying between pH 1 and pH 2 Fig 6 illustrates 2 typical examples

(3) *Achlorhydria*—The third type of abnormal pattern depends on the recognition of achlorhydria, where the pH of specimens is more alkaline than that of Töpfer's reagent (pH 3 5) in most of the samples throughout the twenty four hours, 2 such examples are shown in fig 7 The finding of acid in the last few specimens is not uncommon and succeeded an initial achlorhydria in 9 patients.

These varieties of secretion pattern, obtained in the acute stages of the illness, had a significant relation to the site and type of ulcer, and were sufficiently clear to be of diagnostic value In 13 patients, however, the acid values obtained were not abnormal, the achlorhydria, observed consistently in the postoperative group, reflected the disturbance in gastric function following operation and was of no diagnostic use. The frequency distribution of secretion patterns between gastric, duodenal, and acute ulcers and hiatal lesions is shown in fig 8. Of 31 patients showing high night acidity, 27 proved later to have chronic duodenal lesions, 14 of 18 patients showing nocturnal neutralisation had chronic gastric ulcers, and, perhaps most significant of all, the finding of achlorhydria distinguished the acute ulcers, because 32 of 36 patients showing this phenomenon were finally recognised as having bled from an acute ulcer Of 4 patients with hiatal lesions 1 had high nocturnal acidity, 2 had achlorhydria, and 1 had normal night acidity

The finding of normal night acidity in 13 patients was of no diagnostic importance, being evenly distributed among the various types of ulcer, and the achlorhydria invariably found in the 7 patients of the postoperative group was clearly of no significance The reliability of the secretion patterns in the remaining 85 patients is indicated in table III, a correct diagnosis being achieved in 73 (85 9%) Reliable diagnostic information was obtained in 14 of 18 patients showing nocturnal neutralisation (77 8%), in 27 of 31 showing high night acidity (87 1%), and in 32 of 36 patients with achlorhydria (88 9%), statistical tests show these findings to be significant in all groups

The difference between the groups can also clearly be seen by calculating the mean pH values observed at



5—In 2 patients bleeding from chronic gastric ulcer reductions in nocturnal acidity approximating to alkaline levels.

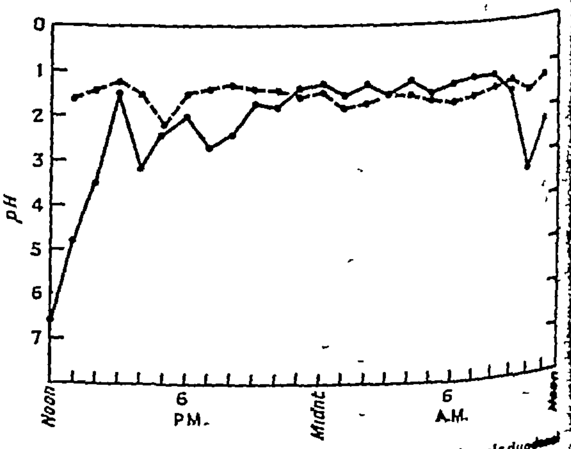


Fig 6—High night acidity in two patients bleeding from chronic duod ulcers.

each hour in the patients studied. Hunt (1952) has described averages of pH values as "means of the negative logarithm of hydrogen ion concentration which have no physiological or clinical meaning" Whatever may be the mathematical limitations of these values they serve as efficient units of comparison between the groups of patients studied. In fig 9 the hourly mean pH values have been calculated, together with the standard error of the observations. Highest values were present in the patients with chronic duodenal ulcer and ranged between pH 2 33 (± 219) and pH 3 29 (± 421), with high nocturnal acidity, at no time was a pH of 3 5 exceeded In the patients with chronic gastric ulcer alkaline values ranging between pH 3 94 (± 482) and pH 5 14 (± 517) were observed at night, coinciding with nocturnal neutralisation in most of these patients. In patients with acute ulcers mean pH values were significantly more alkaline than pH 5 5 at all hours ranging between pH 4·13 (± 259) and pH 5 42 (± 249)

A further demonstration of group variations is afforded by the comparison of the number of hours when pH values more alkaline than pH 3 5 were recorded. Patients with chronic duodenal ulcers were achlorhydric for a mean of 6 26 hours (± 1 131), with chronic gastric ulcers for a mean of 9·76 hours (± 1 314) and with acute ulcers for a mean of 17 95 hours (± 1 229) The application of Student's 't' test to these data shows highly significant differences between the patients with the acute and those with *chronic duodenal ulcer* (*t* = 3 526, *n* = 75 *p* = <0·001) and significant differences between the patients with acute and those with chronic gastric ulcer (t = 2 741 n = 57 p = <0·01) There is no significant difference between those with chronic duodenal ulcers and those with chronic gastric ulcers (t = 1 229, n = 50, p = <0·3)

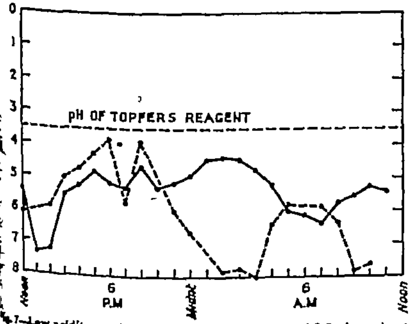


Fig 7—Low acidity persistently more alkaline than pH 3 5 throughout 24 hours in 2 patients bleeding from acute peptic ulcer

A second gastric analysis was made in 45 patients some weeks after hæmorrhage had ceased. High night acidity persisted in 10 of 12 patients who had originally shown this type of secretion pattern. Nocturnal neutralisation was again demonstrated to be a phasic phenomenon (Watkinson 1951) disappearing in 5 of 7 patients in whom the analysis was repeated. Return of acid secretion occurred in 20 of 23 patients initially achlorhydric at the time of hæmorrhage Fig 10 demonstrates this change in 2 of these patients.

Discussion

The difficulty in correctly diagnosing the cause of the hæmorrhage has been recognised in previous reports dealing with hæmatemesis, especially in the acute stages. We feel that hourly gastric aspiration facilitates diagnosis. The inadequacy of present diagnostic methods assumes considerable importance when we attempt to

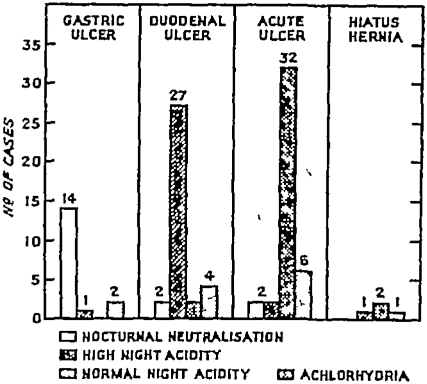


Fig 6—Relation of secretory patterns to ultimate diagnosis. Most of the gastric ulcers showed nocturnal neutralisation, whereas high acidity preponderated among patients with duodenal ulcer A significant proportion of patients with acute ulcer had achlorhydria.

assess the significance of an abnormally acid gastric secretion, and it must clearly bear on the validity of our conclusions in this report. Radiological and operative confirmation is forthcoming in patients with chronic gastric and duodenal ulcers but not in those with acute ulcers. Thus Needham and McConachie (1950) could give only an approximate estimate of the proportion of their hæmatemesis patients who had bled from acute peptic ulcer A high standard of diagnosis has been achieved by Tanner (1950) and Avery Jones (1952) largely by early gastroscopy combined with surgery and radiography Similar detailed investigation has been used in the present series, in which the distribution of the types of ulcer resembles that of the larger series reported by these workers

The mortality has been low only 3 patients dying of the 105 treated (2 9%): 1 in the fourth postoperative week from pulmonary embolism 1 on the fifth day from coronary thrombosis necropsy revealing in addition wide dissemination of carcinoma from a primary growth in the lung while the death of 1, a man of 88 could fairly be attributed to hæmatemesis, though carcinomatosis and chronic lung disease were important contributing causes. The mortality rate was not bad compared with the larger series of Avery Jones (1952) and Tanner (1950) but the numbers are small

This procedure allows of the prompt recognition of recurrence or continuance of bleeding When the physician is guided by his observations of the pulse rate and blood pressure, resuscitative measures are only too often applied tardily We have made it a rule that the nurses inform the house-officer when the aspirated specimens reveal recurrence of bloodstaining whatever the

TABLE III—RELATION OF SECRETION PATTERN TO FINAL DIAGNOSIS

Secretion pattern	No. of patients	No. with correct diagnosis	No with incorrect diagnosis	Difference	S.E. of difference of proportion
Nocturnal neutralisation	18	14(77 8 %)	4	0 556	0 113
High night acidity	31	27(87 1%)	4	0·742	0 103*
Achlorhydria	36	32(88 9%)	4	0 778	0 101
Total	85	73(85 9%)	12	0 717	0·075

Results significant.

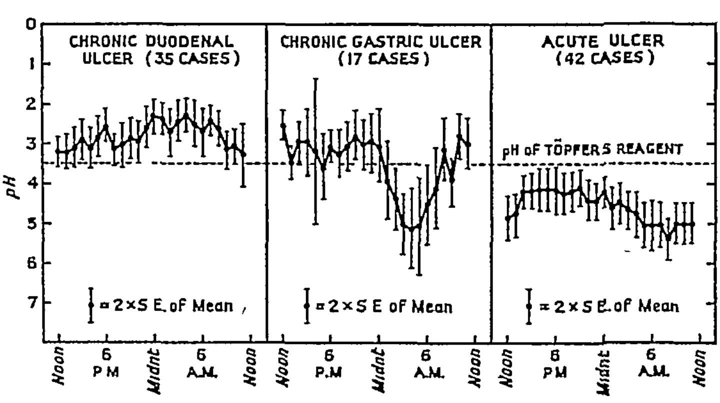


Fig 9—Mean hourly pH values with standard error Note highest nocturnal acidity with chronic duodenal ulcers and contrast with low nocturnal acidity with chronic gastric ulcers With acute ulcers mean pH values are significantly more alkaline than pH 3 5 at all hours.

clinical state of the patient is judged to be , thus the necessary preparations for transfusion can be made and treatment planned in advance In some patients the site of the hæmorrhage can be deduced from the association of continuing melæna with clear aspirated specimens The simple bedside observation of bloodstaining can provide reliable information both about recurrent bleeding and ulcer site, and with Kinsella (1950) we advocate its wider application

The changes observed in intragastric pH immediately after hæmorrhage have been of diagnostic value in 73 of the 85 patients in whom the secretion patterns were abnormal The finding of high night acidity facilitated accurate diagnosis in 27 of the 35 patients with chronic duodenal ulcers, this secretion pattern being usual in ulcers of this type uncomplicated by hæmorrhage Nocturnal neutralisation was observed in 14 of 17 patients with chronic gastric ulcers, a higher proportion than is commonly found with the uncomplicated lesion (Watkinson 1951), and again providing diagnostic information in a significant number We have come to attach great importance to the presence of achlorhydria, because 32 of the 36 patients with achlorhydria were finally classed as having an acute ulcer These results enable a more confident assumption to be made of the cause of the bleeding than would otherwise have been possible, especially in hæmorrhage from acute peptic ulcer, where the recognition of achlorhydria provides an indication for continued medical treatment,

We have been fortunate in the surgical assistance at our disposal, for of the 19 patients submitted to emergency gastrectomy only 1 died—in the fourth postoperative week from pulmonary embolism Severe recurrent hæmorrhage may demand operation even though a firm preoperative diagnosis of acute peptic ulceration has been made, based on the finding of achlorhydria This happened in 5 patients in whom operation verified the diagnosis and to whom a total of 73 pints of blood had been transfused before operation was advised Optimal conditions for successful surgery require an early decision in suitable patients, particularly those acknowledged subjects of chronic peptic ulceration where bleeding has recurred We believe *that this method can aid in their* early selection

The finding of achlorhydria in bleeding acute ulcer has not previously been described, the mechanism of its production is far from clear and many possible factors merit consideration Neutralisation of the stomach contents with blood appear of first importance, but the aspirated specimens were bloodstained as commonly with chronic as with acute ulcer Further, wide fluctuations in intragastric pH were observed despite uniformly bloodstained specimens, as is shown in fig 2, where the pH varied between pH 1 6 and pH 8 0, although all the specimens contained fresh blood

The *introduction of blood into the normal* stomach has various effects The isolated instillation of a large quantity produces only a short-lived achlorhydria, but the repeated introduction of moderate amounts causes a more uniform depression of acid secretion approximating to achlorhydria This observation suggests that the achlorhydria accompanying bleeding acute ulcer results from long continued oozing of blood from the submucosal vessels, in contrast to the more dramatic but isolated event of arterial bleeding in chronic ulcer

TABLE IV—RELATION OF ACHLORHYDRIA TO CLINICAL SEVERITY

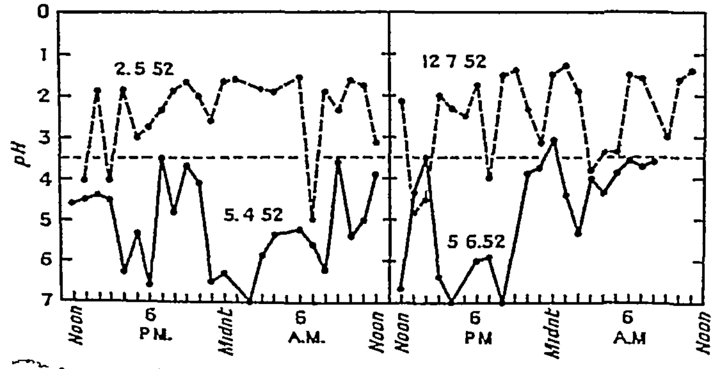
Severity	Chronic ulcer		Acute ulcer		Difference	S.E. of difference of proportion
	Achlorhydric	Not achlorhydric	Achlorhydric	Not achlorhydric		
Severe	1	14	12	3	0 733	0 156*
Moderate	1	20	13	2	0 719	0·164*
Mild		16	7	5		
Total	2	50	32	10	0 796	0 051*

* Results significant.

The effect of shock with accompanying fluid depletion and hypotension cannot be held entirely responsible for the genesis of achlorhydria A clinical assessment of severity on admission proved more satisfactory than a comparison of the amounts of blood transfused to each group, which, besides indicating the requirements of resuscitation necessary on admission, reflected also the number and severity of recurrent hæmorrhages If the numbers of patients with achlorhydria and either acute or chronic ulcer are studied in relation to the clinical severity on admission (table IV), it will be seen that, at all degrees of severity, the proportion showing achlorhydria was far higher among patients with acute ulcer than among those with chronic ulcer this difference being significant

The influence of plasma bicarbonate and blood urea levels on gastric secretion has been investigated by Apperly (1936) and Conway (1952) These levels were estimated many times in the present series and appeared in no way related to the abnormal secretion pattern obtained.

There remains the hypothesis that a difference in secretion, between patients



of acid secretion in 2 patients with acute ulcers initially achlorhydric at time of hæmorrhage.

acute and patients with chronic ulcer is ultimately responsible for the changes observed The difference in age and sex incidence between the groups is well known, and mucosal differences may well be present. Rodgers and Avery Jones (1938) have shown that acute ulcers are often accompanied by atrophic gastric mucosa, observed at gastroscopy, and hypochlorhydria as judged from a Rehfuss test-meal given at an unspecified time after hæmorrhage. The findings of Vanzant et al. (1932) who demonstrated an increasing incidence of achlorhydria with advancing age, might suggest that age and sex are concerned in the production of achlorhydria. Of the 16 males with acute ulcer and achlorhydria 15 were aged less than 60 and 9 less than 45 Of the 16 females with acute ulcer and achlorhydria 10 were aged less than 60 and 6 less than 45 These figures do not suggest that in these patients achlorhydria was related to age

Though the mechanism of the secretion variations remains unexplained, it is thought that gastric aspiration in the acute stages of gastroduodenal hæmorrhage has proved a safe and informative procedure and has aided materially in the management of the patients investigated

Conclusions

Early hourly gastric aspiration in 105 patients with hæmatemesis yielded valuable information and proved harmless

The bedside observation of bloodstaining in the aspirated specimens was useful because further hæmorrhage could be detected before other clinical criteria had indicated its presence; its absence sometimes aided localisation of the ulcer

A study of the acidity of aspirated specimens has shown that high nocturnal acidity is usual in bleeding chronic duodenal ulcer that nocturnal neutralisation is commoner in bleeding than in uncomplicated gastric ulcer and that achlorhydria is observed at the time of hæmorrhage in acute peptic ulceration, the acid often returning after several days observation

Achlorhydria in the acute stages of gastro intestinal hæmorrhage is thought to be an added indication for continued medical treatment.

Possible causes of the achlorhydria are discussed.

Our thanks are due to Prof. S J Hartfall Prof. R E Tunbridge, Dr Maxwell Telling and Dr R N Tattersall for allowing us to study patients admitted under their care and to Mr G Armitage Mr M. C Oldfield, Mr A. J C. Latchmore, Mr H. S Shucksmith, Mr D B Feather Mr H. Moore and Mr A. V Pollock, who operated on some of the patients studied. We should like to thank Mr D W Coulson for technical help Without the assistance of the nursing staff of the General Infirmary at Leeds and of St. James s Hospital Leeds, the investigation would not have been possible We are grateful to Professor Hartfall and Professor Tunbridge for their criticism and to Dr Maxwell Telling for his help in the preparation of this paper

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LACTATION AND FLUID INTAKE

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IT is customary to advise mothers in the early days of the puerperium, and at other times if there is an insufficiency of milk, to drink a lot of fluid to increase the milk-supply It seemed to one of us (R. S I) that it was unlikely on physiological grounds, that mothers would produce more milk if they took more fluid than they felt the desire to take It seemed likely that thirst, often experienced when the baby begins to suck is nature s method of supplying fluid needs in lactation, and that additional fluid is unnecessary A controlled experiment was therefore planned, on the same lines as a previous investigation (Illingworth and Stone 1952) to decide this question.

TABLE I—NUMBERS OF BABIES IN FORCED FLUID AND ORDINARY FLUID GROUPS IN DIFFERENT BIRTH WEIGHT CLASSES

Birth weight class (¼ oz. units)	Forced fluid group		Ordinary fluid group	
	Wards 1 and 3	Wards 2 and 4	Wards 1 and 3	Wards 2 and 4
350 (5 lb 7½ oz.)–399	5	4	6	5
400 (6 lb 4 oz.)–449	8	18	8	13
450 (7 lb ½ oz.)–499	22	10	22	23
500 (7 lb. 13 oz.)–549	13	7	13	9
550 (8 lb 9½ oz.)–599	6	8	4	1
600 (9 lb 6 oz.)–649	1	2	1	—
650 (10 lb. 2½ oz.) or more	1	—	1	—
Total	56	49	55	51

Method of Study

Maternity cases are nursed on two floors in the Jessop Hospital Each floor is divided into two wards, each ward being under the charge of one sister Two pædiatricians one on each floor, are responsible for the care of the babies with one pædiatric registrar or senior house-officer It was felt that there might be unrecognised differences in the management of lactation in the various wards so it was arranged that in one ward upstairs and one ward downstairs the mothers were asked to drink at least six pints of fluid a day from the first day onwards, with instructions to continue doing so when they returned home. In the remaining two wards one upstairs and one downstairs, no mention

TABLE II—COMPARISON OF BIRTH WEIGHTS, FLUID TAKEN BY MOTHERS PARITY, AND INCIDENCE OF BREAST FEEDING IN TWO WARDS

—	Average birth weight (¼ oz. units)	Average daily amount of fluid taken by mother (oz.)	Percentage of multiparæ	Percentage of babies fully breast-fed	
				On discharge	At age of 1 month
Forced-fluid group					
Wards 1 and 3	485	105·2	27·3	81·8	70·4
Wards 2 and 4	480	110·0	20·4	83·7	73·3
Ordinary-fluid group					
Wards 1 and 3	482	66·8	29·1	87·3	81·0
Wards 2 and 4	465	71·6	19·0	86·3	70·0

TABLE III—AMOUNT (OZ) OF FLUID TAKEN BY MOTHERS IN EACH OF FIRST 9 DAYS

—	Day								
	1	2	3	4	5	6	7	8	9
Ordinary-fluid group	61 0	69 0	67 9	67 1	67 8	71 4	73 1	73 3	70 2
Forced fluid group	85 0	102 8	108 8	109 0	110 7	113 4	114 3	115 1	110 0

at all was made about fluid intake, even if there were an insufficiency of milk, the mothers being left to take what they desired Only full-term babies were included in the study, but otherwise there was no selection of babies, all being included. When 50 complete records had been obtained in each pair of wards, the arrangement was to be changed over, so that the pair of wards in which fluids had been pushed now allowed the mothers to take only what they desired, and vice versa

The following records were kept the weight of the baby at birth, the weight on the 3rd, 5th, 7th, and 9th days and at the age of 1 month, the amount obtained by test feeds throughout the 8th day, added to that which was expressed after each feed, the amount of fluid taken each day by the mother in the first 9 days, and the incidence of full breast feeding, complementary feeding, and artificial feeding in hospital and at the age of 1 month

TABLE IV—GAIN IN WEIGHT ON 9TH DAY IN RELATION TO BIRTH WEIGHT

Birth weight group	Forced fluid group		Ordinary fluid group		Student's t test for difference between means
	Mean weight above birth weight (oz)	No of babies	Mean weight above or below birth weight (oz)	No of babies	
A	+0 07	22	+1 26	19	0 88
B	−1 00	35	−1 15	47	0 09
C	−2·03	27	−0 90	26	1 00

In all, 106 mothers were left to drink only what they desired (the “ ordinary-fluid group ”), and 104 mothers were asked to take at least six pints a day (the “ forced fluid group ”)

For part of the study the babies were divided into three birth-weight groups, as follows

Group A, birth weight less than 6 lb $13^{1}/_{4}$ oz

TABLE V—AVERAGE GAIN IN WEIGHT OF BABIES BY 3RD, 5TH, 7TH, AND 9TH DAYS

Day	Forced fluid group		Ordinary fluid group		Student's t test for difference between means
	Mean weight above or below birth weight (oz)	No of babies	Mean weight above or below birth weight (oz)	No of babies	
3	− 7 99	95	− 7 93	101	0 15
5	− 6 18	95	− 5 49	101	1 27
7	− 3 77	92	− 3·05	97	1 21
9	− 1 11	84	− 0 58	92	0 78

Group B, birth weight from 6 lb $13^{1}/_{4}$ oz to 7 lb 13 oz inclusive

Group C, birth weight greater than 7 lb 13 oz

COMPARABILITY OF THE TWO GROUPS

Birth weight—The birth weights of the babies studied were shown to be comparable (tables I and II) in the two groups of wards

Other Data—Table II shows that the parity of the mothers, the incidence of breast-feeding, and the amount of fluid taken were comparable in the two groups of wards Since there is no significant difference in these data from the two wards, the results from the two ward can henceforward be combined

Results

Amount of Fluid Taken—The average amount o fluid taken by the 106 mothers in the ordinary flui group was 69 1 oz, and by the 104 mothers in th forced-fluid group 107 5 oz Table III shows the averag amount taken by the mothers in each of the first 9 day We have no records of the amount of fluid taken by th mothers on return home Any such figures woul inevitably be inaccurate

TABLE VI—CORRELATION COEFFICIENTS BETWEEN AVERAG DAILY AMOUNT OF FLUID TAKEN AND GAIN IN WEIGHT 5TH AND 9TH DAYS

—	Day 5		Day 9	
	Coefficient	Number	Coefficient	Numbe
Ordinary fluid group	+ 0 12	101	+ 0 02	92
Forced fluid group	− 0 09	95	− 0 16	84

Gain in Weight—Table IV shows the gain in weigh in the two groups in relation to the birth weight Ther are no significant differences in any of the three birt weight groups A, B, and C When similar tables ar calculated for the weight gains by other days, there i again no significant difference, nor is there an difference when all the babies are classed togethe irrespective of their birth weight (table V) The fac that the number of babies studied on the 7th and 9t days is smaller than on the 3rd and 5th days is due t the necessity of excluding figures for gain in weight i a complementary feed was given Complementary feed were not given before the 6th day

Correlation Between Gain in Weight and Amount o Fluid Taken—Table VI shows the correlation betwee the gain in weight on the 5th and 9th days and the average daily amounts of fluid taken up to those days. There is apparently no linear relationship between the amount of fluid taken and the weight gain, and even when both groups are taken together no relationship of any kind exists Table VII shows that there is no significant difference in the gain in weight of the babies in the two groups at the age of 1 month in relation to their birth weight

TABLE VII—AVERAGE WEIGHTS OF BABIES AT AGE OF 1 MONT

Birth weight group	Forced-fluid group		Ordinary fluid group		Student's t test for difference between means
	Mean weight at 1 month (oz)	No of babies	Mean weight at 1 month (oz)	No of babies	
A	123 8	17	125 1	20	0 37
B	141 4	35	140 2	44	0 54
C	156 1	28	158 8	19	0·62

Test Feed (8th day)—Table VIII shows the results of test feeds in the mothers in the two groups. The only difference of significance is that in group C (the largest babies) More milk was produced by the mothers in the ordinary fluid group than in the forced-fluid group

TABLE VIII—TEST FEEDS FOR FORCED AND ORDINARY FEEDING

Birth weight group	Forced fluid group		Ordinary fluid group		Student's t test for difference between means
	Mean test feed (oz)	No of babies	Mean test feed (oz)	No of babies	
A	15 28	25	14 97	24	0 21
B	15 02	42	15 19	54	0 59
C	15 20	37	18 26	28	2 63*

* Result significant at 5% level.

TABLE IX—CORRELATION COEFFICIENTS BETWEEN AVERAGE DAILY AMOUNT OF FLUID TAKEN AND TEST FEED

—	Correlation coefficient	Number
Ordinary fluid group	+ 0 15	100
Forced-fluid group	− 0 20*	104

* Result significant at 5% level.

Correlation between Amount of Fluid Taken and Test Feed.—Table IX shows the correlation between the average daily amount of fluid taken by the mothers and the result of the test feed on the 8th day The correlation coefficient in the forced fluid group is just significantly negative This seems to suggest that there is a stage when too much fluid may have a detrimental effect on the supply of milk Both groups were combined to test for a curvilinear regression of the test feed on the amount of fluid taken but the result was not significant

Incidence of Full Breast-feeding on Discharge and at Age of 1 Month.—Table X shows that there is no significant difference in the two groups

Discussion

TABLE X—NUMBERS AND PERCENTAGES OF BABIES FULLY BREAST FED ON DISCHARGE, AND AT AGE OF 1 MONTH

—	Fully breast-fed	
	On discharge	At age of 1 month
Forced-fluid group	86/104 (*82 7*%)	64/89 (*71 9*%)
Ordinary fluid group	92/106 (*86 8*%)	69/92 (*75 0*%)

This investigation showed that not only does the forcing of fluids have no beneficial effect in increasing milk production, but also that it may have a harmful effect and reduce it. We therefore feel that the widespread custom of trying to persuade mothers to drink large quantities of fluid during lactation should be abandoned.

After completion of the investigation one of us (R S I) searched 48 volumes of the *Quarterly Cumulative Index Medicus* for other work on this subject and could only find a single investigation described in two papers by Olsen (1940 1941), who pointed out that, if it were true that forced fluids increased milk production one might also expect a corresponding increase of other body secretions, such as tears and saliva, when additional fluids are taken, this is not known to happen He remarked that there is no evidence that cows produce more milk when given extra water to drink Olsen made a careful study of 13 nursing mothers, giving them widely varying quantities of fluid, from 600 ml to 3775 ml a day, and doing daily test feeds to determine whether there was any correlation between the amount of fluid taken and the amount of milk produced. The quantity of fluid was then changed several times in these mothers, so that those who had been given large amounts of fluid were given very small amounts, and vice versa. There was no correlation at all between the amount of fluid taken by the mothers and the amount of milk produced. Five mothers became very thirsty on restricted fluids, but there was no decrease in the quantity of milk produced, and in 1 there was an increase Olsen concluded ' Forced excessive drinking is therefore neither necessary nor as a rule, beneficial as far as the nursing is concerned, and may even be harmful ' Our investigation adds support to Olsen's views.

Morrison (1952) mentions two other papers on the subject. Macy et al. (1930) found no correlation between milk volume and fluid intake in 3 subjects. Lelong et al. (1949) found no significant difference in the milk produced by a woman in a 10-day period in which 1322 ml. water was given per day and in an 11-day period in which the average water intake was 445 ml. There was no difference in the percentage of fat, protein, or carbohydrate in milk in the two periods

Summary

A controlled investigation was made on the relati ship of fluid intake to the amount of milk produced 210 mothers in a maternity unit.

106 mothers were given no instruction about h much fluid they should take, being left to drink w they wanted. The average daily amount of fluid dr by them was 69 1 oz.

104 mothers were instructed to take at least 6 p of fluid a day ; the average daily quantity taken them was 107 5 oz

The gain in weight of the babies, the result of t feeds, and the incidence of full breast-feeding w observed, the babies being divided into three birth wei groups

There was no evidence that the forcing of fluids h any beneficial effect on lactation On the contra there was evidence that more milk was produced mothers who only drank enough to satisfy their needs.

When the amount of fluid taken by all the moth was correlated with the test feeds, there was a significa negative correlation coefficient in favour of letting t mothers satisfy their fluid needs without being asked take more fluid.

The practice of instructing lactating women to dri large quantities of fluid should be abandoned Th should merely take enough to satisfy their own desires.

We wish to thank Miss M. J W Taylor, matron of t Jessop Hospital, and all the nurses and sisters who so willin coöperated in the investigation, which would have be impossible without their help We also wish to thank Dr Colver pediatrician, some of whose patients were includ in the study

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INTENSIFIED ELECTROCONVULSANT THERAPY

REVIEW OF FIVE YEARS EXPERIENCE

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IN the five years since two of us described intensifie electroconvulsant therapy (Page and Russell 1948) w have treated more than 3500 further cases involvin more than 15,000 treatments.

Many critics seem to have a wrong conception of th method and believe that the patient receives to separate treatments in one day We therefore emphasis that the course normally consists of one treatment daily and is not given twice a day except in the severest case

The method originally consisted in giving an initia stimulus of 150V for one second. This stimulus wa immediately followed by seven further stimuli of on second each at 150V at intervals of half a second Th number of extra stimuli was increased by one at subsequent daily treatments, up to ten on the fourth day

More recently we have increased the number of extra stimuli, and aim to give sufficient in each case to maintain the tonic phase long enough to take the place of, and eliminate, the clonic phase of the fit The number required varies with different patients, and is usually between eight and fifteen The lower number is sufficient in an elderly patient, whereas a young schizophrenic may require fifteen or more The elimination of the clonic phase may also be achieved with a continuous stimulus of from ten to fifteen seconds, but we have found that the interrupted stimuli are more effective clinically

Contrary to what one would expect, these extra stimuli do not increase the severity of the fit but render it smooth and shorter

The daily repetition of the treatment until the symptoms have cleared is an essential part of the method

It has been stated by some critics of intensive electroconvulsant therapy, without any experience of the method, that it is dangerous and causes "cerebral damage" In our experience it is less dangerous than ordinary electroconvulsant therapy The risk of fractures is much less, since the clonic phase is eliminated in most cases, and for this reason we only use "muscle relaxants" in those few cases where a known risk of fracture exists We have seen no clinical evidence of "cerebral damage" following the normal use of intensive electroconvulsant therapy The degree of amnesia and confusion following treatment varies from case to case, but it is no greater than that following a comparable number of ordinary electroconvulsant treatments

The indefinable fear of electroconvulsant therapy which so many patients experience after the ordinary treatment is almost unknown after the intensive treatment We believe this is because subconvulsive stimuli are impossible with intensive electroconvulsant therapy, and it is now rare for a patient to object to a further course of treatment when this is required

Treatment of Depressives

The depressive case undoubtedly shows the best response to all forms of electroconvulsant therapy, and provides a suitable basis for comparison of methods We are indebted to many other hospitals and psychiatrists who have given us data for this comparison

An important factor is the interval between treatments Most users of ordinary electroconvulsant therapy appear to favour intervals of two to seven days, and it is significant that the shorter interval gives improved results judged by the lower number of treatments required (table I)

TABLE I—EFFECT OF INTERVAL BETWEEN TREATMENTS

Type of electroconvulsant therapy	Frequency of treatments	Usual no of treatments required per case of depression
Ordinary	1 a week	10–15
	2 a week	7–10
	3 a week	6–8
	Daily	5–7
Intensified	Daily	3–4

The degree or depth of depression in each case determines the number of treatments required Whereas two intensive treatments are sufficient in a mild depressive, a severe agitated melancholic may require as many as six or seven daily treatments It is in these severe cases that intensive electroconvulsant therapy shows to particular advantage, and we have seen many such cases that have failed to respond to ordinary electroconvulsant therapy which have successfully responded to intensive treatment

In our original series of cases the average number of treatments per case for all depressives was 3 2 This figure has now risen slightly to nearly 4 per case, because we find that giving one extra treatment after the depression has apparently cleared assists in preventing relapses

Skill and experience are required to judge when treatment should be stopped, and we find that, when in doubt, it is well to give one more treatment to prevent relapses.

Each case should be judged individually, and no fixed number of treatments should ever be contemplated.

We find that the predominantly exogenous and predominantly endogenous types of depression respond equally well to intensive electroconvulsant therapy, but the exogenous type usually requires slightly more treatments per case Similarly, the patient at the beginning of a depressive phase requires more treatments than one near the end of a depressive phase Since a good response is almost a certainty with intensive electroconvulsant therapy there seems to be no justification for leaving a patient to suffer days of depression while waiting for the declining phase

We treat most of our mild and moderately severe depressives as outpatients, and, since they require only three or four treatments, it is possible for them to return to work within a week or less of the start of treatment.

Puerperal Psychosis

TABLE II—RESULTS OF DIFFERENT TREATMENTS IN PUERPERAL PSYCHOSIS

Therapy	No of cases	No of deaths	Average stay in hospital (weeks)	No remaining in hospital	Average no of treatments per case	No. of cases relapsing	Failures
Other than electro convulsant	41	5	110	7	—	3	36·6%
Ordinary electro convulsant	7	0	27	1	11	2	42 8%
Intensive electro-convulsant	54	0	12	0	5 5	2	3 7%

A dramatic change has taken place in the prognosis of puerperal psychosis with the introduction of intensive electroconvulsant therapy We have treated 54 such cases and have compared them with the records of 41 similar cases before the days of electroconvulsant therapy and with 7 cases treated with ordinary electroconvulsant therapy (table II) All these patients were admitted to hospital within three months of parturition

We do not consider that puerperal psychosis is a separate entity, but believe it is a mental breakdown due to antenatal and postnatal stresses in a psychotically predisposed person

Before the introduction of electroconvulsant therapy 5 of 41 patients died and 7 are still in hospital as chronic psychotics after more than fourteen years Of those discharged the average length of stay in hospital was more than two years

Only 7 patients were treated with ordinary electroconvulsant therapy before the development of intensive treatment in 1946 These 7 patients show some improvement over those not treated by electroconvulsant therapy, but 1 has remained in hospital as a chronic case, and the average stay in hospital was still twenty seven weeks.

With intensive electroconvulsant therapy there have been no deaths, and none of the patients remains in hospital The average stay in hospital for the whole 54 patients was twelve weeks, but 2 of them were in for just over a year If these 2 cases are omitted, the average stay was seven weeks

Table II also shows the number of cases in each group that relapsed and were readmitted to hospital within two years of original discharge The failures are expressed as a percentage of each group, and include relapses, deaths, and those remaining in hospital The apparent high percentage of failures with ordinary electroconvulsant therapy is undoubtedly due to the small number of

, and would probably have been about 25% with
ger number

e number of intensive treatments given varied
een two and ten per case, with an average of 5 5
ared with the 11 per case with ordinary electr
ulsant therapy Treatment was begun within
ty four hours of admission to hospital and in 3 cases
irst treatment was given within forty-eight hours of
ntion.

lphonamides or antibiotics were not used in any of
ases.

e deaths before the use of electroconvulsant therapy
ar to have resulted from exhaustion due to the
nts' overactivity and inability to take fluids and
shment. These factors are readily overcome by
sive electroconvulsant therapy

e believe that early intensive treatment is important
ese cases because the early removal of psychotic
toms seems to prevent the development of chronic
hosis.

Schizophrenia

ulin-coma therapy has been continuously practised
is hospital for eighteen years. Looking back over
many schizophrenics of all types that have been
ed with insulin coma, one realises how disappoint
ineffective this treatment has been when the cases
ollowed up for five or more years Undoubtedly
results are seen occasionally in carefully picked
but for the whole group the most one can expect
emission of up to two years. These remissions may
peated with further courses of insulin in some cases,
he ultimate prognosis is very poor

ith this in mind we have during the past five
, treated most of our schizophrenics with intensive
roconvulsant therapy

ily treatments are started as soon as the patient is
tted and we find that acute schizophrenic symptoms
be rapidly cleared with four to seven treatments in
cases. Where patients have lost weight the
sive electroconvulsant therapy is immediately
wed with a course of modified insulin therapy to
ove the physical condition

ere appears to be no satisfactory way to present the
ts of treatment of schizophrenia statistically but our
ession after five years is that the results of combin
of intensive electroconvulsant therapy and modified
in therapy are as good as, and possibly superior to
e obtained previously with insulin coma alone

ny of the mild schizophrenics without any physical
ioration have been treated as outpatients with
sive electroconvulsant therapy alone This has
led many to continue a useful economic life for
ral years, with maintenance treatments at intervals
x to twelve months when necessary

Chronic Psychosis

e have used intensive electroconvulsant therapy
nsively for chronic psychotics, and particularly good
lts have been obtained with the disturbed and
ted types. We estimate that the destruction rate of
ing bedding, windows, &c. is now less than 20%
he rate before the introduction of electroconvulsant
apy Similarly, the number of patients now able to
nd hospital entertainments and recreations has
tly increased.

he use of protection rooms and seclusion is now
paratively rare, and is limited to the short interval
ween the patients' outburst and their receiving
tment. Tube-feeding and the use of special clothing
e been eliminated, and the strain on a depleted nursing
f has been noticeably decreased.

Ethics of Electroconvulsant Therapy

o have electroconvulsant therapy is a major event in
tient's life, and it is too easy for the operator to regard
it as a routine affair We think it very important that no patient should ever see or hear other patients undergoing treatment. We deplore the use of the term "shock treatment" and always describe it simply as "electrical treatment" to patients and their relations.

Patients are very ready to spread alarming tales of the treatment among each other Hence we always prefer to begin the treatment of new cases within twenty four hours of admission to hospital. Since the physical contra-indications for electroconvulsant therapy are now so few, it is seldom that this routine cannot be adhered to

Cerebral Stimulation

During the last year cerebral stimulation has been used as a "counter stimulus" immediately following intensive electroconvulsant therapy in 43 cases of depression

This stimulus is applied in the same way as electroconvulsant therapy and consists of a unidirectional interrupted direct current at 50 cycles per second With a strength of 5–7 mA applied for two to three minutes the effect is to reduce considerably postoperative amnesia and confusion It also appears to have a calming influence on the patient and thereby reduces anxiety and tension.

There seems to be a tendency for "counter stimulus" to reduce the effectiveness of electroconvulsant therapy slightly and we find that it is often necessary to give one more electroconvulsant treatment than would have been expected if "counter-stimulus" had not been used Counter-stimulus is most useful in depressed patients of high intellect who are anxious to return to work as soon as treatment is completed.

Counter-stimulus is definitely contra-indicated in schizophrenia and hysteria because the symptoms do not clear when it is used This suggests that the development of some amnesia is an important factor in the clearance of symptoms in cases other than depressives.

Conclusion

Intensive electroconvulsant therapy is not a new treatment but a technique of applying electroconvulsant therapy in those cases where it is indicated We believe its greater effectiveness over ordinary electroconvulsant therapy is due to the fact that larger stimuli are given in a shorter time

Many of those who have not seen the technique believe it to be a drastic form of treatment, but this fallacy is dispelled when the method has been observed. It seems that, apart from those visitors to whom we have demonstrated the technique, few have attempted it.

Patients appreciate intensive electroconvulsant therapy because it offers better results in a shorter time and has largely overcome the fear reaction to electroconvulsant therapy Electroconvulsant therapy should never be applied indiscriminately but properly applied it is probably the greatest advance so far made in psychiatry

Summary

Intensive electroconvulsant therapy with recent developments, is described

The effect of varying the frequency of treatments is discussed.

The comparative results in the treatment of puerperal psychosis with intensive, with ordinary, and without electroconvulsant therapy are given.

The use of intensive electroconvulsant therapy in schizophrenia and in chronic psychosis is discussed

The use of "counter-stimulus" after electroconvulsant therapy is described.

Ectron apparatus, which we believe to be the only type suitable for intensive electroconvulsant therapy was used throughout our work, and we are indebted to Ectron Ltd., of Baldock, Herts, for the loan of a cerebral stimulator

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FUMAGILLIN IN AMŒBIASIS

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M A, M D Camb, M.R C P

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We have previously shown that antibiotics are useful in the control of the acute phase of amœbic colitis (Armstrong et al 1949, 1950, Elsdon-Dew et al. 1952) Though there is little doubt that this action has in the main been through the associated bacterial flora, there was some suggestion that some antibiotics might have a slight amœbicidal action

The isolation of fumagillin by Hanson and Eble (1949) quickly led to a study by McCowen et al. (1951) of its properties, including a lethal effect on *Entamœba histolytica* in vitro, with no apparent effect on the bacterial flora, and with a corresponding curative effect on experimental amœbiasis in animals These results were confirmed by Hrenoff and Nakamura (1951) using cultures in association with *Trypanosoma cruzi*

The application of fumagillin to human cases soon followed

Killough et al (1952), using up to 50 mg daily in 22 cases, in which 12 patients had no symptoms, 9 had mild gastro intestinal disturbance, and 1 had severe amœbic dysentery, reported parasitic clearance in all but the severe case, in which apparently a liver abscess developed

Anderson et al (1952) treated 20 chronically infected cases of amœbiasis with fumagillin, using a total divided dose of up to 100 mg in twelve days, and reported relapse in 6 out of 10 cases on a smaller dosage and in 1 out of 10 on a larger dosage They did not observe any signs or symptoms of intolerance

Steigmann et al (1952) treated two different series of cases with fumagillin In the first series, of 11 chronic and 4 acute cases, 4 patients given 200 mg daily were cleared of amœbæ but developed untoward symptoms, such as exfoliative dermatitis and psychosis, and 11 patients given 100 mg daily had moderate nausea with occasional vomiting, 3 of them developing a macular rash on the face and extremities All 15 were parasite free at the end of therapy, but 5 relapsed within three months. In the second series, of 25 cases, of 5 "carriers" given 150 mg daily for ten days 2 were parasite-free at the end of three months, of 10 "carriers" given 100 mg for ten days 7 were negative after three months, and in 10 active cases of amœbiasis treated with 120 mg daily for ten days there were 4 failures.

Present Series

Our unit has been active in the assessment of drugs in the treatment of amœbiasis A plethora of cases of acute amœbic colitis allows us to select patients for trial therapy on a strict and uniform basis, details of which have been reported elsewhere (Elsdon-Dew et al 1952) Assessment at the twentieth day is made on the following basis

Success —Symptom free, all ulcers healed, and no amœbæ found in stools

Possible Failure —Usually symptom free, one or more ulcers still open, but amœbæ not found in stools or in scrapings.

Absolute Failure.—Open ulcers still present and amœbæ still demonstrable

Removed from Treatment —Patients showing severe clinical deterioration were placed on therapy known to be effective Where this deterioration took place before the fifth day, such cases were not included in the series, but after the fifth day such cases are shown as "removed from treatment."

COMPARISON OF RESULTS OBTAINED WITH DIFFERENT DRUGS IN AMŒBIASIS

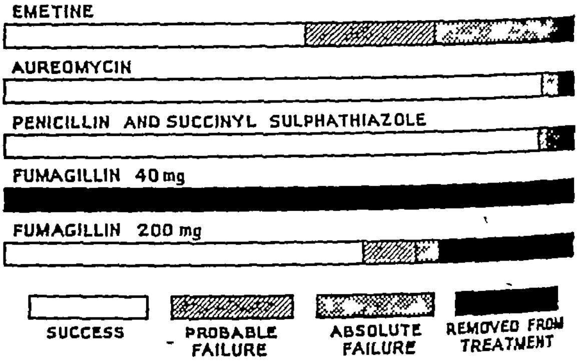
Treatment	No of cases	Success (%)	Probable failure (%)	Absolute failure (%)	Removed from treatment (%)	Total absolute failure (%)
Emetine	50	50 0	22 0	28 0		28 0
Aureomycin	52	92 3	3 8	1 9	1 9	3 8
Penicillin and succinyl sulphathiazole	50	92 0	2·0	4 0	2 0	6 0
Fumagillin 40 mg	7				100 0	100 0
Fumagillin 200 mg	48	62 4	6 3	4 2	27 1	31 3

Dosage and Toxicity

Two series of cases have been treated, one of 7 cases on fumagillin 20 mg twice daily for ten days, and one of 48 cases on fumagillin 50 mg four times a day for 10 days

Systematic laboratory examinations to assess possible toxicity were not made, but the patients complained of no untoward symptoms except an irritative fine desquamating rash on the face This happened only on the larger dosage of 200 mg a day

Of 49 patients who received fumagillin 200 mg a day 14 developed facial dermatitis, which appeared between the sixth and tenth days For this no treatment was given other than calamine lotion, and the fumagillin therapy was continued The dermatitis subsided spontaneously within five days after the end of fumagillin therapy



Comparison of results obtained with different drugs in amœbiasis.

Results

In the accompanying table and figure the results are summarised and compared with those obtained with emetine, with aureomycin, and with penicillin and succinyl sulphathiazole

Of the patients treated with fumagillin 40 mg daily, 3 were removed from treatment because of clinical deterioration before completing the course The remaining 4 patients all showed ulceration and parasites after completing treatment with fumagillin Assay, by the manufacturers, of the activity of the fumagillin remaining after this series had been treated, showed a 28% loss.

Of the patients treated with the larger dosage, 3 were removed from treatment on the fifth, sixth, and seventh days owing to clinical deterioration before completing their course, and because it was felt unjustifiable to withhold known effective treatment

At ten days from the start of treatment 28 cases were classified as successes and 10 as probable failures The remaining 7 were absolute failures with open ulcers and free forms of *E histolytica* and were removed from this series

Before final assessment at twenty-seven days from the start of treatment 2 further cases became absolute failures and were consequently given other treatment 2 cases persisted as probable failures with open ulcers and no parasites demonstrable As both patients complained of diarrhœa with blood and mucus they were treated with emetine, 'Diodoquin,' and phthalylsulphathiazole, with relief of symptoms One patient complained of severe diarrhœa with much blood and mucus at enty *days from the start of treatment*, *although no* ers or parasites were seen, the symptoms demanded her treatment, and the case was consequently removed om this series.

Of the remaining 33 patients 31 had no symptoms, ers, or parasites at twenty-seven days from the start treatment and were discharged from hospital 2 were mptom free and no ulceration was seen on sigmoid copy, but cysts of *E histolytica* were found in their ols. No other treatment was given, but unfortunately ese patients have not returned for follow up The rican is reluctant to return to hospital unless he feels . Consequently our follow up has been very inadequate

Conclusions and Summary

Fumagillin 40 mg daily was ineffective in controlling ute amoebic dysentery

Fumagillin 200 mg daily for ten days produced ults comparable to those obtained with emetine gr 1 ily for ten days but inferior to those obtained with reomycin 2 g daily for fifteen days.

The only toxic action observed was a mild facial rmatitis which only occurred with the larger dosage

These results apply only to acute ulcerative amoebiasis the African male

Our thanks are due to the Council for Scientific and Indus al Research and the Natal Provincial Administration for eir continued support, and to the Upjohn Company of lamazoo for supplies of fumagillin and for their ready operation in the assay of the remaining material

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ACUTE SALT DEPLETION ASSOCIATED WITH THE NEPHROTIC SYNDROME

DEVELOPING DURING TREATMENT WITH A MERCURIAL DIURETIC

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ALTHOUGH many toxic actions of mercurial diuretics re well known, those affecting the kidney have been nly rarely described Of these descriptions most relate o slight and transient toxic manifestations such as he finding of casts, leucocytes, or erythrocytes in the rine, and mild albuminuria (deGraff and Nadler 1942) nd it is not always clear to what extent these findings re due to the underlying disease. However two cases ith severe renal tubular involvement have been noted by Waife and Pratt (1946) and Bruno (1948) It was considered of interest to report the present case firstly because of the severe renal tubular damage found post mortem for which there is substantial evidence incriminating the mercurial diuretic 'Neptal and secondly because the patient presented with a severe sodium and chloride depletion similar to that found in a crisis of Addison's disease, associated with the clinical and biochemical picture of the nephrotic syndrome.

Case report

A woman aged 54 had been admitted seventeen months previously to the London Hospital with an anterolateral cardiac infarct, thought to be extensive on electrocardiographic evidence This was associated with some degree of left ventricular failure, shown by orthopnoea, and medium crepitations at both lung bases. On treatment with the mercurial diuretic neptal 2 ml. intramuscularly twice a week for the first week, and thereafter once a week symptoms disappeared in a few days. The blood pressure varied between 110/75 and 140/100 mm. Hg The urine on admission contained a haze of protein. This disappeared on the third day and frequent subsequent analyses revealed no abnormality Fifteen months previously the treatment with neptal was discontinued, and the patient was seen regularly thereafter in the outpatient department. After a month attacks of paroxysmal nocturnal dyspnoea occurred. These improved after treatment with neptal 2 ml. intramuscularly once a week, but did not disappear until the same injection was given twice weekly The patient remained symptom free on this treatment, leading a normal life for her age Occasional examination of the urine during this period revealed no proteinuria. There was no dietary restriction of salt the daily intake being estimated at about 5 g In all, 130 injections of neptal 2 ml were given in sixty-eight weeks. A week previously the patient had noticed progressive swelling of ankles and face particularly of eyelids, and felt very weak. This was followed two days later by vomiting two or three times a day accompanied by some anorexia. During this week two injections of neptal were given by the patient's family doctor with good diuresis after the first but not after the second injection. The second injection was given forty-eight hours before admission to hospital. No further relevant information was obtained from the previous, family, or social history

On examination the patient was obviously ill but coöperative with her mental state clear and no dyspnoea at rest She had a pale face and cyanosis of her lips, and of her hands and feet which were cold and clammy There was considerable oedema of legs sacrum, face, and arms. The blood pressure was not recordable The pulse was regular but scarcely palpable, pulse-rate 92 per min The jugular venous pressure was not visibly raised The apex beat was at the fifth left intercostal space in the anterior axillary line (as on the previous admission); the heart sounds were distant and no thrills or murmurs were detected. No abnormality was detected in the respiratory system, abdomen, or central nervous system.

Investigations —Electrocardiography showed evidence of old cardiac infarct. Radiography of the chest showed an opacity at the left base suggesting a small pleural effusion. The urine contained much protein, when it had been boiled at pH 4 and had stood for an hour nine-tenths of its original volume was occupied by precipitated protein. Microscopy of the deposit showed a few red cells, leucocytes, and granular casts. On culture the urine was sterile It contained urea 21 g per litre chloride 43 m.eq per litre, sp. gr 1 025 The plasma chloride level was 86·5 m.eq per litre, plasma-sodium level 108 m.eq per litre plasma-potassium 4 71 m.eq per litre blood urea level 75 mg per 100 ml. total plasma-protein level 4 1 g per 100 ml., plasma-albumin level 1·6 g per 100 ml. plasma-globulin level 2 5 g per 100 ml. blood-cholesterol level 570 mg per 100 ml. and hæmatocrit 54%

Treatment and progress —A daily total of $2^{1}/_{2}$ litres of sodium-chloride solution (155 m.eq of sodium chloride per litre) was given by mouth for two days, in addition to a semisolid diet and adequate amounts of water This the patient took well, with no further vomiting Her blood pressure became recordable at 90/60 mm. Hg on the second day In spite of this her condition had clearly deteriorated and the oedema had much increased. On the third day the plasma chloride level was 79 m.eq per litre, plasma-sodium level 120 m.eq per litre plasma-potassium level 4 37 m.eq per litre and hæmatocrit 57%. Urinary chloride in a random specimen was 10 5 m.eq of sodium chloride per litre An intravenous drip of sodium-chloride solution (155 m.eq of sodium chloride per litre) was set up and 10 ml. of adrenal cortical extract (Eucortone) was given intravenously every four hours. There was no obvious improvement after twelve hours. 750 ml of 6% dextran solution was then administered slowly by intravenous infusion. The patient's condition rapidly improved; her limb extremities became warm and pink for the first time and her blood pressure rose to 130/90 mm. Hg But the peripheral oedema had again increased Four hours later pulmonary oedema supervened, and death took place two days later No further blood for analysis could be obtained, owing to the oedema The twenty-four hour urine volumes for each day except the last three were about 1200 ml In the last three days the volumes diminished, the lowest being 300 ml on the last day of life The specific gravities varied between 1 005 and 1 025 Each specimen contained much protein.

Necropsy

Necropsy was done three days after death, the body being kept in the cold chamber The principal findings were confluent purulent bronchopneumonia, severe degeneration of the kidneys, and an old infarct of the myocardium Œdema of the feet, legs, and lumbar pad was noted

Heart —The lower four fifths of the anterior wall of the left ventricle and adjacent interventricular septum were replaced by fibrosis, the adjacent pericardial sac being obliterated by fibrous adhesions. The lumen of the lower half of the anterior descending branch of the left coronary artery was occupied by organised thrombus There was severe general atheroma of the aorta and its branches

Kidneys —Combined weight 319 g The subcapsular surfaces were smooth, the cortex swollen and greyish yellow, with congested straight interlobular vessels, there was slight blurring of the junction between cortex and medulla, the latter showing a few yellow streaks in the apices of the pyramids Small groups of petechial hæmorrhages mottled the pelvic mucosa The rest of the urinary tract appeared normal

Endocrine glands —All appeared normal apart from post mortem degeneration, with central softening, in the suprarenal bodies (combined weight 16 8 g) Microscopically there was abundant sudanophil lipoid in much of the suprarenal cortex, especially its deeper layers, the degeneration present appeared attributable to post-mortem changes The pituitary was microscopically normal

Spleen —There was diffuse congestion attributable, microscopically, to acute inflammation of the pulp

Liver —Parenchymatous degeneration and, microscopically, slight periportal fatty change, no congestion.

Microscopic Examination of Kidneys

The cortex was unevenly congested, some glomeruli being engorged and others bloodless In a good many of the glomeruli the capsular epithelium had undergone severe degeneration, with desquamation of the cells and the formation of collections of eosinophil flocculent debris in the capsular space In other respects the glomeruli appeared normal

Severe degenerative changes were found in the tubules, especially the convoluted segments The epithelium of the first convoluted tubules and of the descending thick part of the loops of Henle was pale, swollen, and finely vacuolated, in a few tubules the degeneration had proceeded to necrosis Stages of karyolysis and pyknosis were obvious The lumina were reduced and often contained eosinophil debris In frozen sections part of this vacuolation was accounted for by sudanophil doubly refractive droplets, presumably cholesterol esters, which were conspicuous in the basal part of these cells. Since stains for glycogen were negative, the remainder of the vacuolation was attributed to hydropic degeneration.

In the distal segments there was considerable desquamation of the epithelium, suggesting post-mortem degeneration. But in places it was clear that ante mortem degeneration had led to loss of the cells, since there was clear evidence of epithelial regeneration Thus, in these tubules, desquamation was accompanied by a flattened lining of basophilic cells in which the nuclei were unevenly distributed Bulky hyaline and granular casts occupied many of the lumina both here and in the collecting tubules, in a few of the second convoluted tubules there were collections of polymorphs A few leucocytes were also found in the thin loops of Henle, nuclear pyknosis and karyorrhexis affected the epithelium also at this level

The interstitial tissue was oedematous A few groups of lymphocytes lay beneath the kidney capsule and near large veins in the upper medulla Elsewhere an occasional polymorph was found Apart from hypertrophy and fibrosis of the intima of the arcuate and interlobular arteries there were no vascular changes

Discussion

The clinical features of this case up to a week before the patient's second admission are not remarkable A cardiac infarct sustained seventeen months previously was associated at the time with some degree of left ventricular failure This subsided with rest in bed and neptal injections The injections were subsequently discontinued Three months later, attacks of paroxysmal nocturnal dyspnœa supervened The attacks were well controlled with further injections of neptal twice weekly The patient remained symptom free on these injections for fourteen months No other treatment was given. There was no restriction of salt in the diet

However, the clinical features dating from the week before her second admission are unusual They can clearly be divided into two well-recognised syndromes (1) the syndrome of acute sodium and chloride depletion similar to that seen in the crisis of Addison's disease, with weakness, vomiting, thready pulse, low blood pressure, cold extremities, raised hæmatocrit, raised blood urea level, and lowered plasma sodium and plasma-chloride levels, but with a moderate concentration of chloride in the urine, and (2) the nephrotic syndrome commonly associated with type II nephritis (Ellis 1942), characterised by œdema of the legs, arms, and face, profuse proteinuria, lowered plasma-protein level, the albumin fraction being particularly affected, and a raised blood cholesterol level

A sodium and chloride depletion of the magnitude here observed could only have been caused by a loss of Na and Cl ions from the body Possible routes in this patient would be via the vomit and the urine However, the vomiting was not profuse, and the plasma-electrolyte levels did not suggest an electrolyte depletion due to vomiting, the Cl ion being less depleted than the Na ion. No obvious cause of vomiting as a primary symptom was found either clinically or post mortem It is much more likely that the vomiting was the result of a sodium and chloride depletion rather than the cause It will be noted that other symptoms preceded the vomiting by two days

It is therefore likely that sodium and chloride were lost by urinary excretion, and this is strongly supported by the finding of 43 m eq per litre of chloride in the urine on admission forty eight hours after the last neptal injection Possible causes of urinary loss of sodium and chloride are (1) Addison's disease, (2) the diuretic phase of acute tubular necrosis (Bull et al 1950), (3) "salt losing nephritis" (Thorn et al 1944, Joiner and Thorne 1952), and (4) the action of the mercurial diuretic Addison's disease can be immediately excluded by the normal plasma potassium level, the failure to respond to adrenal cortical extract, and the normal adrenal glands at necropsy The diuretic phase of acute tubular necrosis can similarly be excluded There was no previous anuria and no recognisable cause for anuria There was no subsequent polyuria (the urine-urea level was 21 g per litre on admission), and the electrolyte depletion affected mainly the Na and Cl ions, whereas in acute tubular necrosis K is usually also involved Previously reported causes of "salt losing nephritis" can be excluded by the necropsy findings

There remains the action of the mercurial diuretic It is well recognised that a sodium depletion can follow the use of mercurial diuretics (Schroeder 1949, Soloff and Zatuchni 1949), but it only seems to do so when the diuretics are given in conjunction with a low sodium diet (Schroeder 1949), with ion exchange resins, or when the diuretics are given daily, especially in elderly persons (Jaffe et al 1950) In the present case the diet was normal, salt was not restricted, no ion exchange resins were given, and the diuretic was not administered more often than twice weekly The sodium and chloride depletion here observed was far more severe than in most of the cases previously reported, and was associated with the nephrotic syndrome, which complicated none of those cases It therefore appears unlikely that the condition here observed is directly comparable with these simple low sodium states

In view of the presence of the nephrotic syndrome, the possibility must be considered that type II nephritis might be a contributory factor The onset of this disease ot, however, associated with a sodium and chloride etion of any magnitude

hese clinical features suggest that they may be ciated with a diffuse renal lesion, of which the main lence is in the tubules, and for which the mercurial etic might be responsible A predominantly tubular n could account for the renal loss of sodium and ride, from failure of adequate tubular reabsorption hese ions. The development of the nephrotic syn no is more difficult to explain Tubular necrosis due poisoning with inorganic mercurial salts does not lly produce this picture (Fishberg 1939, Volhard l). However, the occurrence of this syndrome due he action of an organic mercurial diuretic is not nded and must be regarded as a possibility

ome support for this view comes from previous unts of severe tubular damage attributable to curial diuretics, where profuse proteinuria and ma have been a feature clinically Two such accounts e been published by Bruno (1948) and Waife and tt (1946)

he case described by Bruno was one of heart-failure with al stenosis. The patient developed nausea vomiting and ma, together with proteinuria and chloride depletion while er treatment with a mercurial diuretic These findings e attributed to toxic nephritis due to the diuretic. ever the patient was a known diabetic and considerable rcapillary glomerulo sclerosis was found at necropsy It erefore doubtful to what extent the clinical features can ttributed to the diuretic.

aife and Pratt (1946) described a case of heart failure with ral stenosis in which the patient was treated with 28 ctions of 'Mercurophylline' in eight months. The patient denly developed oedema of the face and arms, profuse teinuria, and a raised blood urea level The extremities ame cold and the blood pressure unrecordable. Unfortu ely no plasma-electrolyte levels were reported, but the lings of cold extremities, low blood pressure and raised od urea level suggest sodium and chloride depletion. These kers diagnosed toxic nephrosis due to the mercurial retic, and their case appears very similar to ours.

The pathological evidence can now be considered The g interval between death and necropsy was responsible the considerable amount of post-mortem degeneration n on microscopy of the kidneys. This makes it ficult to assess accurately the degree of ante mortem ular degeneration However after due allowance has en made for this factor it is clear that there must have en severe degeneration and even necrosis of the tubule ithelium since evidence of regeneration was found the second convoluted tubules. Analysis, in fact, ggests that this part of the nephron was the most erely affected and this is supported by the focal lymorph infiltration of the lumina in these segments. t the proximal convoluted tubules were also involved was shown by the sudanophil lipoid in their cells It difficult to tell whether the other changes in the oximal convoluted tubules developed before or after ath.

Already published reports of cases in which renal ions are attributed to the use of mercurial diuretics in art-failure agree in describing severe degeneration of e tubule epithelium, sometimes advancing to necrosis osenthal 1933 Waife and Pratt 1946) with evidence regeneration (Sprunt 1930 Waife and Pratt 1946) alcification is sometimes mentioned as an important ature (Tarr and Jacobson 1932) but we have observed onspicuous calcification in the kidneys of young people ith rheumatic carditis and heart-failure who had never ad mercurial diuretics. The production of tubular egeneration by mercurial diuretics in advanced heart-ailure is extremely difficult to prove, owing to the well nown incidence of degeneration in untreated cases. But hen the degeneration amounts to necrosis, with clear vidence of regeneration and where there is evidence of mercurial intoxication from the examination of other tissues (Sprunt 1930, Rosenthal 1933 Waife and Pratt 1946) the likelihood that the lesion is due to the mercurial diuretic appears undeniable The problem in our case is easier because there was no evidence of congestive heart-failure either clinically or post mortem

Further evidence that the mercury ion in both inorganic and organic combination may cause anatomical lesions in the renal tubular epithelium is obtained from previous reports Page and Wilson (1940) have reported the cases of two patients who died on the seventeenth and eighteenth days after the use of a bladder wash of mercury oxycyanide. Microscopically the kidneys in these two cases were similar except for extensive calcification in one The glomeruli were normal, but there was severe degeneration of the epithelium throughout the tubules, with active regeneration

To elucidate certain observed features of human intoxication with organic mercury methyl compounds arising from their preparation as insecticides, Hunter et al (1940) treated rats and a monkey with these substances. Microscopy of the rats kidneys revealed normal glomeruli but severe dropsical and hyaline-droplet degeneration of the epithelium of the convoluted tubules, amounting in places to necrosis The lumina were often blocked by cellular debris There was some evidence of epithelial regeneration Re-examination of the monkey s kidney establishes that the glomeruli were normal Albuminous and dropsical degeneration was conspicuous in the proximal tubules. The distal tubules were more severely affected, with shedding of the epithelium and regeneration

The only finding in the present case that at all suggests type II nephritis is the presence of doubly refractive sudanophil lipoid in the proximal convoluted tubules Probably this was related to the raised blood-cholesterol level. It was not, however, a prominent histological feature, and in all other respects the picture differed from any known form of Bright s disease However glomerular changes in early type-II nephritis (nephritis mitis lipoid nephrosis) are slight and a pre-existing type-II nephritis with tubular necrosis superimposed, cannot confidently be excluded by microscopy

Although it appears unlikely that the sodium and chloride depletion observed in the present case would be responsible for the tubular necrosis, the possibility needs consideration Some evidence on this point can be obtained from an examination of the kidneys in Addison s disease

Although experimentally severe damage can be inflicted on the renal epithelium of rats by total adrenalectomy (Simpson and Korenchevsky 1936) there are no characteristic findings in the kidneys in human examples of Addison's disease (Allen 1952) Ten cases have been reviewed by us including some that had received adequate hormonal treatment and some untreated cases that came to necropsy in the early decades of this century The kidneys in these showed various degrees of parenchymatous degeneration, occasionally fatty involving the tubules diffusely and without special selection of the distal segments. Casts were rare and, when present consisted of a few hyaline deposits in the collecting tubules. In one example alone (an untreated case) was there evidence of regeneration in the distal convoluted tubules. There was no interstitial reaction in the cortex It is clear then, that in man severe sodium depletion can exist without the tubular changes observed in the present case, at least in Addison s disease.

The evidence both clinical and pathological therefore supports the view that the tubular necrosis and severe salt depletion in the present case was due to the mercurial diuretic neptal. In accounting for the nephrotic syndrome the recent onset of type II nephritis cannot be confidently excluded There is, however no positive evidence of this condition either clinical or histological

The low plasma protein level and the high blood-cholesterol level, together with the histological finding of lipoid in the tubular epithelium, does, however, suggest that the condition may have antedated the appearance of the œdema, which was present for only a week before admission

The coexistence of severe sodium and chloride depletion and the nephrotic syndrome is of particular interest Although severe sodium and chloride depletion from renal loss of these electrolytes also occurs in acute tubular necrosis and in "salt losing nephritis," in neither of these conditions is the depletion associated with the nephrotic syndrome Nor, in the development of the nephrotic syndrome, as in type-II nephritis, is the rapid accumulation of œdema usually associated with severe salt depletion

Summary

A case is reported in which acute sodium and chloride depletion, associated with the nephrotic syndrome, developed during therapy with the mercurial diuretic neptal for heart-failure

A severe renal tubular lesion was demonstrated histologically

Evidence is presented which suggests that the mercurial diuretic may have been responsible

We are indebted to Dr A. E Clark-Kennedy for permission to publish this case, and to Prof Clifford Wilson for valuable help and advice

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SPUTUM DISPOSAL IN THE HOME

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'Milsol' (Milton) is a hypochlorite solution containing caustic soda A H Walters (personal communication) has shown that sputum is dissolved in 15–30 seconds when added to this solution This quality suggested that milsol might provide a suitable means of disposal of sputum, especially for patients in their own homes The value of such a process would be greatly enhanced if the sputum was sterilised at the same time

Experimental Observations

Two experiments were performed, their object being (1) to measure the time required by milsol to kill *Mycobacterium tuberculosis*, and (2) to ascertain whether the bactericidal effect of the antiseptic was reduced by prolonged contact with the sputum In these experiments it was assumed that failure to obtain growth of *M tuberculosis* after 10 weeks indicated a bactericidal action

Experiment I

Method —Sputum known to contain large numbers of tubercle bacilli was collected from seven patients All the specimens were mixed together Of this mixture 5 ml. volumes were added to each of 44 sterile 1-oz. screw-capped bottles Of these bottles 4 were used as controls, they were liquefied with trisodium phosphate and inoculated on Lowenstein-Jensen medium, two slopes of this medium being inoculated from each bottle. To each of the remaining 40 bottles 20 ml of milsol was added rapidly, and the bottles were then shaken gently to dissolve the sputum The 40 bottles were divided into 5 groups

Group A, representing a "milsol contact time" of 15 minutes, were centrifuged for 15 minutes at 3000 r p.m. The supernatant fluid was discarded, and the small deposit was resuspended in 25 ml of sterile glass-distilled water After shaking, the contents were neutralised with 8% hydrochloric acid, using bromthymol blue as indicator The bottles were again centrifuged at 3000 r p.m After the supernatant fluid had been discarded, a few drops of tryptone water were added to each deposit, from which two Löwenstein-Jensen slopes were inoculated The slopes were incubated at 37°C for 10 weeks, and cultures were examined each week for evidence of growth

Group B, fifteen minutes after homogenisation, was treated in the same way as group A. This group represented a "milsol contact time" of about 30 minutes.

Group C represented a "milsol contact time" of 60 minutes.

Group D represented a "milsol contact time" of 90 minutes.

Group E represented a "milsol contact time" of 120 minutes.

A surface scum formed in all the bottles of groups C, D, and E Each scum was removed and mixed with 25 ml of sterile glass distilled water After centrifugation at 3000 r p m for 15 minutes each deposit was resuspended in 25 ml of sterile glass distilled water Centrifugation was repeated, and after the addition of a few drops of tryptone water films of the deposit were made for microscopical examination The remainder of the deposit was cultured on two Lowenstein Jensen slopes.

Results —The following results were obtained

Controls

Smears —Acid fast bacilli were present in smears from all specimens

Cultures —All the cultures were positive for *M tuberculosis* after 4 weeks' incubation

Sputa mixed with milsol

Smears —None were made from groups A and B Acid fast bacilli were present in all the smears from groups C, D, and E

Cultures —All the cultures were negative for *M tuberculosis* after 10 weeks

Experiment II

Method —150 ml of milsol was placed in each of six 1-lb jam jars, and 10–15 ml of sputum known to contain large numbers of tubercle bacilli was added. More sputum was added after 1, 2, and 4 hours The jars were shaken after each addition 30 minutes after the last addition of sputum ($4\frac{1}{2}$ hours after commencement) 5 ml of scum was removed and cultured as described in experiment I 2 hours later ($6\frac{1}{2}$ hours after commencement) another 10–15 ml of sputum was added. The jars were then left overnight Next morning (23 hours after commencement) more sputum was added to the jars, and 30 minutes later 15 ml of scum was removed from each, treated as described above, and cultured This procedure was repeated 2 hours later Finally, all the jars were emptied, and swabs for culture were taken from their rims Control smears and cultures were also made from four samples of the original sputum

Results —The following results were obtained

Controls

Smears —Acid fast bacilli were present in smears from all the specimens

Cultures —All cultures were positive for *M tuberculosis* after 4 weeks' incubation.

Sputum mixed with milsol

Smears —Acid fast bacilli were present in all the smears *ultures.*—All the cultures were negative for *M tuberculosis* after 10 weeks incubation

bs from rims

ultures.—All the cultures were negative for *M tuberculosis* after 10 weeks incubation.

Conclusions

Milsol was found rapidly lethal for *M tuberculosis* and longed contact with sputum did not significantly luce its bactericidal properties for this organism

Milsol quickly dissolves sputum and these qualities gest a simple technique for the disposal of sputum in home Using two receptacles a routine may easily devised which ensures bactericidal action by milsol. e adoption of this technique should satisfy both thetic and bacteriological requirements

SPOSAL OF TUBERCULOUS SPUTUM IN THE HOME A NEW METHOD

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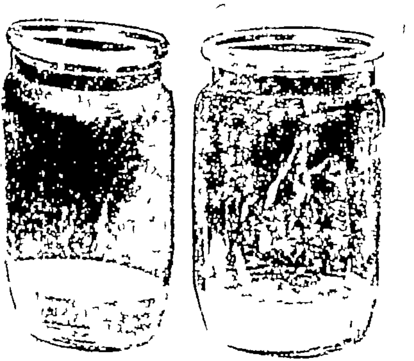
THERE are at present three main methods of disposing the sputum of tuberculous patients (1) the use of a g which contains a disinfectant (e g Lysol) and must cleaned and sterilised daily (2) the use of paper ndkerchiefs which can be thrust into a paper bag by e bedside; and (3) the use of small disposable cartons patients with more copious sputum or by any patient m whom a specimen is needed. The infected handker iefs and cartons are easily destroyed by incineration. is is the cleaner and probably safer method but utum mugs are still used freely In the home when special facilities for cleaning sterilisation, or inciner ion are available, all these methods become most nsatisfactory

The Milton Deosan Research Laboratory have pro iced an antiseptic ('Milsol) which can be of con iderable value in the disposal of sputum in the home. he basis of the fluid is a modified hypochlorite solution wo fundamental claims are made for it: the sputum is mogenised, with the result that the bacilli are freed to the fluid and no tenacious particles remain and e bactericidal action is of a high order even for tubercle cilli.



(a) (b)

Two jam-jars containing equal quantities of sputum added fifteen minutes previously to (a) milsol and (b) 1:20 carbolic acid.

Personal communication with Dr R W Riddell, of the bacteriological department of Brompton Hospital satisfied me that, *under laboratory conditions* the bactericidal and homogenising actions of milsol were highly effective Formed tenacious sputum was changed in the receptacle into a relatively clear, homogeneous, and sterile fluid easy to dispose of (see figure) Although milsol was satisfactory in the laboratory, it seemed essential that a field trial should be undertaken in the patients own homes under ordinary conditions Such a trial is reported here

Method

All patients using milsol were issued with the maker s instructions as follows:

> "Place 1–3 oz. of milsol in the sputum container (a 1 lb. jam jar is very suitable) according to the amount of sputum normally produced. The fluid in the jar will be quite clear at disposal time if the amount of milsol has been adequate Add more as necessary
>
> After each expectoration rotate the container so that the milsol washes the sides, keeping them clean and free from sputum particles. At the end of 24 hours, and before disposal, leave the container one hour after the last sputum has been added.
>
> Rotate the container and empty the contents down the lavatory Wash it thoroughly in two pints of water to which half a teaspoon of milsol has been added (use a plastic spoon) Add further milsol and return to use

Further explanation was given to the patients by the health visitors as necessary

Trial

Altogether 41 separate investigations were undertaken on 25 patients producing adequate quantities of sputum These patients were provided with milsol, instructed in its use and asked not to empty the sputum pot but to keep a 24 hour specimen for collection by the health visitor In addition they provided one specimen of untreated sputum (for control) expectorated at some time during the same 24 hours as the rest of the sputum was deposited in the milsol fluid.

There was an interval of 1 or 2 hours between collection of the specimens and investigation in the laboratory which was done as follows

(1) *Control sputum.*—Each specimen was treated with 4% sodium hydroxide and centrifuged, and the deposit was washed with distilled water 1 loopful of the deposit was added to a Löwenstein-Jensen slope

(2) *Milsol.*—20 ml of the fluid was centrifuged, and a loopful of the deposit was added to a Löwenstein-Jensen slope.

(3) *Jars*—The inner surface of the top of each jar was swabbed out with a throat swab The swab was treated with 4% sulphuric acid, neutralised, and rubbed on the surface of a Löwenstein-Jensen slope.

All the cultures were incubated for 8 weeks, and the results were read in terms of the degree of growth (maximal +++)

Results

Of the 41 control samples of sputum in the trial 11 yielded no organisms. By providing 1–3 positive sputum samples each, 18 patients yielded the 30 positive results (16 +++ 10 ++ 3 + and 1 with only two colonies)

All the cultures taken from the inside of the 30 jars provided by the sputum positive cases proved negative, as also did 28 of the 30 milsol fluids investigated. There remained 2 milsol samples from which positive cultures were obtained (from a +++ sputum and a ++ sputum) Both these cultures, however provided very scanty growth, only one colony being present on one slope and six on the other Thus only seven colonies of tubercle bacilli were cultivated from a bulk of milsol fluid which contained 30 24-hour specimens of positive sputum 26 of which had yielded heavy growth when cultured directly

Discussion

Non-homogenising disinfectants are bacteriologically unsatisfactory in sputum mugs because unchanged sputum particles can contain living bacilli even though they have been in contact with the disinfecting agent for many hours Adequate cleaning and sterilisation of the sputum mug thus entail daily treatment with soda and subsequent boiling The results reported for the above described simple method, however, appear excellent, particularly when it is realised that, in the case of the 2 milsol positives obtained, the patients involved had very copious sputum and had not added additional milsol to ensure a clear residual fluid There is little doubt in my mind that these fluids also would have been negative, had the patients followed the instructions more carefully In view of this finding I will in future recommend patients to add at least 4 oz of milsol to a 1-lb jam jar (a third of its capacity) to ensure adequate homogenisation and sterilisation of the sputum

Apart from the good bacteriological results obtained, milsol also proved satisfactory æsthetically Most patients, as well as those relations who were acting as nurses in the home, were enthusiastic about this method of disposing of the sputum, the repulsive duty of disposal and cleansing of receptacles had been superseded by a simple, rapid, and safe process

Some patients objected to the smell, and one found that his asthma was aggravated when he leant over the pot to expectorate In addition there is the danger of bleaching carpets and bed-clothes if the milsol is spilt It should be remembered also that only glass or inert plastic containers can be used, because of milsol's corrosive action A 1-lb jam jar is satisfactory and easily replaceable at no cost in any home

There is no doubt whatsoever that milsol represents a great advance on the non-homogenising antiseptic fluids commonly used in sputum containers and at the same time is no more poisonous *It could with advantage* take the place of these not only in the home but also in hospitals using a sputum-mug method of disposal, since there would be less risk of infecting the nurses Milsol also appears to have advantages, particularly at home, over paper handkerchiefs which are expensive, inadequate when there is copious sputum, and need a fire during the summer

Summary

A new antiseptic fluid, 'Milsol,' has been subjected to a small clinical field trial in the homes of tuberculous patients

Milsol proved bacteriologically satisfactory and homogenised sputum, facilitating the cleansing of sputum receptacles

It was acclaimed by those involved as a simple and æsthetically acceptable procedure

This trial has thus shown that milsol has great advantages over other known methods for disposing of tuberculous sputum in the home

My thanks are due to Dr D A Mitcheson and his laboratory staff for the bacteriological work involved, Milton Antiseptic Ltd, who introduced this method and supplied the milsol, and my health visitors for their wholehearted coöperation in the distribution and collection of specimens

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"The demand for sedatives and drugs is a reflection on our present civilisation It has been suggested that the broken home, the gangster film, the present insecurity, and the lack of religious and spiritual comfort account for our increase in crime They also account for our craving for medical panaceas for our spiritual discomforts We would cut the *drug bill if we could substitute the priest for phenobarbitone*, spiritual values for vitamins and hobbies for hormones" —'Consultant Physician' *Manchester Guardian*, Nov 23, 1953, p 5

MERCURIAL POISONING IN EARLY CHILDHOOD

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THE following two cases are published as a further warning against giving mercurial teething powders to infants

Case-records

Case 1—A boy, aged 5 months, attended hospital with *pink disease* He had received two teething powders each week for the previous month, each powder containing 52 mg. of calomel Recovery took place slowly but was complete in two months

A year later, at the age of 16 months he began to cut more teeth, and his mother gave him a further teething powder Three weeks *later this was repeated* According to his parents these were all the mercurial powders he had had a friend of the family suspected that others had been given, but this was never proved. Two days after the administration of the last powder the boy's abdomen began to swell and his urinary output to fall, and he was brought to hospital again

Examination revealed a fretful grossly œdematous child with ascites The blood pressure was 120/75 mm. Hg and the urine contained large quantities of albumin but no casts, red blood-cells, or other formed *elements* The blood-urea was 30 mg, the total plasma proteins 4 5 g., the plasma-albumin 1 2 g, and the plasma-globulin 3 3 g per 100 ml.

Course—A sample of urine taken two days after admission contained 90 µg of mercury in 100 ml Twenty three days later, when the boy was receiving no mercurials, it still contained 15 µg in 100 ml The former quantity indicates severe mercurial poisoning The child went steadily downhill and died seven weeks after admission During this time the urine remained loaded with albumin but without any gross hæmaturia The plasma albumin level remained constantly below normal and below that of the globulin, and the blood-urea remained within normal limits until eighteen days before death, when it rose to 80 mg per 100 ml The clinical picture was that of a nephrosis

Necropsy showed gross œdema of all tissues, with free fluid in the serous cavities. The kidneys were enlarged, weighing 220 g, the glomeruli were excessively cellular, and rare crescent formation had taken place The proximal tubules were normal, and the distal convoluted tubules and the collecting tubules showed some regeneration and peri-tubular fibrosis The blood vessels were normal. The final pathological diagnosis was glomerulotubular nephritis of some weeks' standing with no evidence of mercurial poisoning

Chemical analysis of the organs gave the following results

Organ	*Weight examined* (g)	*Mercurial content* (µg)
Kidneys	220	220
Liver	285	280
Intestines	120	10
Stomach	70	30
Heart	55	20
Femur	75	Trace only

The estimated total amount of mercury in the body at death seven weeks after the cessation of all mercurial administration was 5 mg, equivalent to gr $^{1}/_{10}$ of mercurous chloride

Case 2—A boy, aged 6 months, was referred to hospital because of occasional vomiting for fourteen days and almost complete refusal of food for four days He had received one-quarter of the same mercurial teething powders as case 1 (i e, about 13 mg) every night for the previous three months He had been vaguely off colour for the same time

Examination showed him to be underweight for his age—10 lb 6 oz He was remarkable for his extreme misery and perpetual restlessness He continually pulled and scratched his skin, and he caused sores on his heels by rubbing his feet together and against the bed clothes His eyes were kept half closed, as if the light were painful to them, and whenever possible he rolled into the prone position and buried his head in his pillow, the only position in which he could sleep. His skin was clammy and cold and his extremities were cyanosed but not pink. Hypotonia was marked, but tachycardia was absent ucal diagnosis of pink disease was made and a specimen e was sent for mercurial analysis before treatment . Unfortunately on the sixth night in hospital he y collapsed and died. During his short stay in hos s urine contained only a trace of albumin, without cess of cells or casts. The blood-cells were normal ne contained 404 µg of mercury per 100 ml.

opsy, delayed for twenty four hours revealed no gross in any organ, and microscopy of the kidneys showed nite changes that could not be attributed to post- n changes.

ical analysis of the liver showed 3300 µg of mercury ug and Nelson s method or 5900 µg by Simonson s l in 145 g of tissue The kidneys contained 18 500 µg cury by Laug and Nelson s method or 17 500 µg onsen s method in 45 g of tissue

Discussion

evidence that the administration of mercury to n may be incriminated in a number of pathological ions is increasing Warkany and Hubbard (1948) ered abnormal quantities of mercury in the urine of 41 children with pink disease Since this on was not shown by all the children exposed to the those workers suggested that pink disease may be ersensitivity reaction to mercury The evidence is explanation and a very full examination of the subject is contained in a later report (Warkany Iubbard 1951) The association of pink disease ercurial poisoning has been confirmed by Bivings ewis (1948), Carithers (1949) and Holzel and (1952) The last named, working in this country abnormal quantities of mercury in the urine of 94 cases of pink disease.

it severe renal disease can be caused in children ronic mercurial poisoning from calomel in teething ers has been demonstrated in 5 cases in this country, f them fatal (Wilson et al 1952) Unfortunately cropsy was allowed.

likely is calomel to cause disease that Continental ers write of calomel disease and describe the and allergic effects due to it (Fanconi et al 1947)

zel and James found that of a series of infants ding Manchester and Salford infant clinics some had received mercurial teething powders and 3 consecutive children under the age of 3 years ding the casualty department of the Royal Liver Children s Hospital 130 had received teething ers, of which 94% contained calomel 51% of the pool children receiving powders containing calomel had these one or more times each week during the d of administration

far as case 1 is concerned the evidence that the disease was due to mercurial sensitivity is purely mstantial. That mercury had been given is itted, but there is no evidence that abnormal amounts ercury were present in the body or excreted in the when the baby had pink disease That severe curial poisoning had taken place during the later is evident from the amounts of mercury found e urine and in the organs post mortem. The clinical re was one of nephrosis, but the histological picture that of glomerulonephritis. Was this an ordinary gic glomerulonephritis following a previous infection possibly aggravated by the mercury or was it an gic reaction to the mercury itself? Though the r possibility may be remote it seems unwise to lude it, particularly as other allergic reactions to rcury are known It may be relevant that glomerular ction in the dog has been shown to be severely inter ed with by mercury (Handley et al. 1949) and rpaneto (1947), using corrosive sublimate, has described ons in guineapigs very similar to those of nephritis.

In case 2 mercurial poisoning was undoubtedly present ring the course of the pink disease grossly toxic quantities of mercury being found not only in the urine but also in the organs after death.

Summary and Conclusion

Two cases of fatal calomel poisoning are described, both of which showed symptoms of pink disease, and one of which showed evidence of severe renal damage Administration of calomel to children seldom leads to gross evidence of disease but severe or fatal illness has occasionally followed it In the absence of any conclusive evidence of the beneficial effects of calomel in small children, and in view of its possible harmful effects its widespread and public sale should be condemned

I would like to thank Dr R W Brookfield for his advice on the presentation of this paper Dr R. E. Rowell and Dr T Black for the pathological examinations, Mr N Heron for the chemical analyses in case 1 and Mrs. D Dean for the analyses in case 2 and a critical examination of the techniques available, and Dr M Tun for the collection of statistics.

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SIMPLE ŒSOPHAGEAL CAST

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M.B Sheff M.R.C.P
SENIOR HOUSE OFFICER

ROYAL INFIRMARY SHEFFIELD

Simple œsophageal casts are extremely rare: only 19 cases have been reported since the condition was first described by Birsch Hirschfeld (1877) Patterson (1935) reviewed 17 cases and added 1 of his own and since then only 1 further case has been reported (Willcox 1949) Reichmann (1890) designated the condition "œsophagitis exfoliativa," and Rosenberg (1892) named it "œsophagitis dessicans superficialis. The sex distribution of this condition is equal, and the ages of the patients vary widely (from 20 to 60 years) There was recurrence of cast formation in 4 cases.

A simple œsophageal cast differs from a cast due to corrosive poisoning; the latter frequently leads to stricture formation (Kauffman 1911) while the former leaves no sequelæ. Diphtheritic œsophagitis has been known to lead to cast formation (Raw 1901) Varying ætiological factors have been mentioned as causes for simple cast formation; Patterson suggests a peculiar exfoliative tendency and cites 1 case with severe generalised eczema (Sligh 1893) In most cases the ætiology is

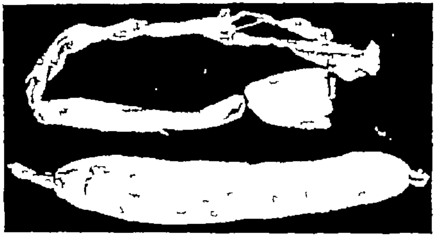

Fig. 1—Œsophageal cast.

obscure although there is often a history of earlier minor œsophageal trauma as in the case reported here

CASE-REPORT

A married woman, aged 35, attended hospital on Jan 4, 1953, complaining of a sensation as of a potato-chip sticking in her throat She experienced this first while eating her evening meal She was examined in the casualty department, and no abnormality was found in the throat or elsewhere She was asked to return for a further examination should the symptom recur A feeling of soreness persisted for a few days but she remained well for seven weeks On Feb 22 she felt a "heaviness" behind the upper sternum, shortly after a breakfast of bacon and tomatoes This was quickly followed by the vomiting of bright red blood, and of a whitish tube She felt that she was choking and replaced the tube by pushing it back into her throat and swallowing This manœuvre was temporarily successful but after fifteen to twenty minutes she vomited again and the tube became detached completely from her throat The patient now felt very ill and was alarmed because she thought "the lining of her throat had come away" The family doctor was called in, and found the patient pale, sweating, and complaining of soreness in the throat A sedative was given and the patient advised to take fluids only by mouth The cast was examined and preserved The swallowing of saliva was very painful after the tube had been vomited, and intense retrosternal discomfort was induced by the swallowing of fluid The soreness gradually diminished, and by the time she was admitted to hospital on March 4 she could eat semisolid food with only mild discomfort There was no history of swallowing alcohol or corrosives, or any other toxic substances The meal preceding the vomiting of the cast was regarded by the patient as a normal breakfast Her general health was good and she felt perfectly well between the episode of dysphagia on Jan 4 and the vomiting of the cast on Feb 22 She had had no serious illnesses and there was no relevant family history

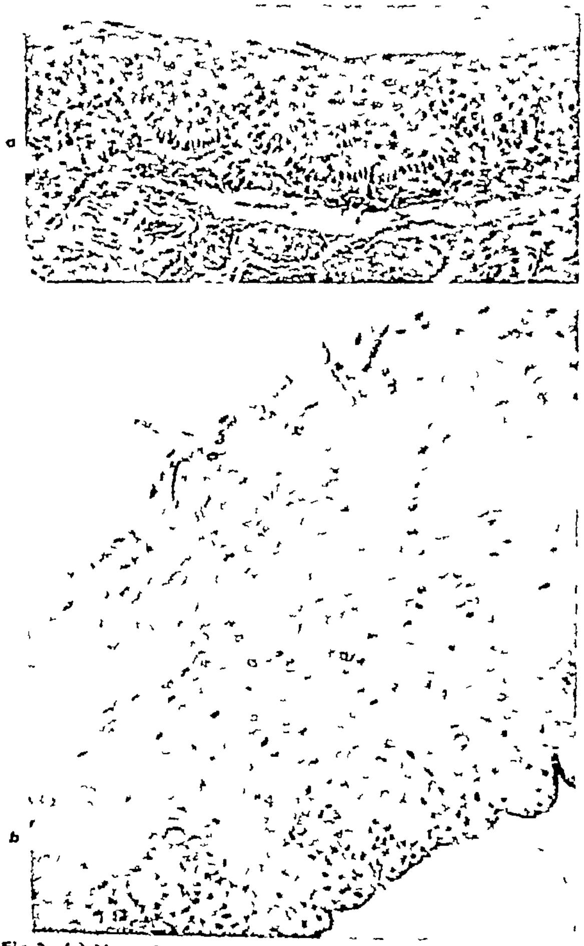

Fig 2—(a) Normal œsophageal epithelium. (b) Section of œsophageal cast (both × 132)

On admission she was pale but not anæmic, and the tongue and fauces appeared normal The blood pressure was 120/70 mm Hg, and no abnormalities were found in any system Œsophagoscopy, sixteen days after the vomiting of the cast, showed a pale atrophic mucous membrane until the œsophagoscope had been passed to 25 cm , beyond this the mucosa was hyperæmic and bled at the slightest touch A barium swallow seven days after the œsophagoscopy revealed no abnormality The blood count was normal , the erythrocyte-sedimentation rate (Wintrobe) was 33 mm in the first hour, the Wassermann reaction was negative

The cast when recovered was a thin walled complete tube so friable that it later broke into two pieces, one 17 5 cm in length the other 14 5 cm , the diameter was 2 cm. (fig 1) The wall was thin, smooth, pearly white, and translucent and showed no red capillary streaks There were no constrictions corresponding to the natural anatomical configurations of the œsophagus Microscopically, it consisted of stratified squamous epithelium, the cells having vesicular nuclei, often surrounded by distinct spaces , there was no infiltration with inflammatory cells The basal layer showed occasional rosettes of cells which probably represented the severed tips of the papillæ (fig 2) The appearances were similar to those described by Patterson and Willcox

DISCUSSION

An œsophageal cast is formed as the result of a split in the wall of the œsophagus , and since it consists entirely of epithelium, the split must occur either through the epithelium or just below the basal layer If the whole epithelium were shed, healing would be by granulation, with scarring and stricture formation , but after a cast has been exfoliated there is rapid and complete recovery Presumably therefore the split occurs through the epithelium, and leaves the œsophagus lined by a thin residual epithelial layer The œsophagoscopy findings in the present case support this view

In an attempt to demonstrate planes of separation we have tried unsuccessfully, in necropsy specimens, to split normal œsophageal epithelium It is not difficult in these specimens to tear off a thin superficial sheet of tissue, but microscopically this artificial cast is seen to consist always of epithelium with an adherent strip of corium A further attempt to split the epithelium has been made by injecting saline through a Mantoux needle as superficially as possible into the wall of a normal œsophagus removed at autopsy Sections of these preparations show that the corium is distended but the epithelium remains intact Normal epithelium is thus difficult to split, so when a cast is formed the epithelium is probably abnormal

In our case the epithelium of the cast is three times as thick as that of a normal œsophagus , microscopically it closely resembles the photomicrographs of the specimens described by Patterson (1935) and Willcox (1949) To investigate whether this thickening was an artefact, a sheet of epithelium and corium stripped from a necropsy specimen was treated in water and spirit, in the same way as the cast This did not swell, and its thickness was unchanged , it merely showed changes due to shrinkage of cells The abnormal appearance of the cast is thus unlikely to be an artefact, and it may be due to epithelial proliferation We have been unable to find any cause for this

A cast may be shed in two ways as a whole, when it is vomited as a coiled intact tube, or as an invaginated tube which is stripped off the wall as the free end passes up the œsophagus, like a sleeve being turned inside out In the second case a section of the cast would show the superficial layer of the epithelium on the outside of the tube Our specimen does not show this, nor do the specimens of Patterson and Willcox The likely sequence of events in these cases was therefore a general loosening of epithelium with exfoliation of a coiled intact tube, The only exception, so far has been recorded by Sclavunos (1893) who noted invagination of a cast, but in this instance the patient vomited a cast shortly after drinking a quantity of industrial spirit, so the case cannot be regarded as typical.

We suggest that the cast is formed in the following manner:

1. Epithelial hyperplasia results from an unknown cause
2. A small split is produced, possibly by trauma, in the abnormal œsophageal epithelium
3. The act of deglutition causes a rise in intra-œsophageal pressure and may gradually cause a progressive dissecting split.
4. New epithelium is growing from the basal layer as the slow dissection proceeds.
5. The final separation of the cast is induced by vomiting

We are indebted to Dr H. P Brody for permission to report this case and for his helpful advice and to the photographic and pathological departments Royal Infirmary Sheffield, for their coöperation

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ISSECTING ANEURYSM OF THE AORTA

RECOVERY AFTER TREATMENT WITH HEXAMETHONIUM

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In the case reported here a patient with dissecting eurysm of the aorta was treated with hexamethonium omide and recovered.

CASE REPORT

A housewife aged 60 who had previously been in good alth, was stricken one morning by a sudden extremely vere pain in the upper abdomen and passing through to e back between the shoulder blades. Almost immediately terwards the pain spread to the right leg which felt cold d useless." The patient said that her husband, feeling e legs, noticed that the right was very cold. There was so some "cramp in the left leg The pain in the trunk sisted throughout the day and she vomited several times. e pain, coldness, and uselessness of the right leg, wever gradually lessened.

On admission to hospital twelve hours later she was still great pain. Her blood pressure was 230/120 mm. Hg in ch arm, and heart-rate 80 regular The apex beat was lf an inch outside the nipple line and at the apex there s a harsh systolic murmur which was also audible along e left border of the sternum. The radial pulses were equal d normal. The right femoral pulse could not be felt e left was palpable though weak. The popliteal dorsalis dis, and posterior tibial pulses were impalpable in both gs. The optic fundi showed narrowing and irregularity of e retinal arteries. The urine sp gr 1 018 contained a oderate amount of albumin but was otherwise normal. The rest of the examination was negative.

Mr. M. H. Hall, the surgical registrar who first saw the tient, made a diagnosis of dissecting aneurysm of the aorta, d she was transferred to the medical side

Investigations

Chest radiography showed an enlarged left ventricle and oss unfolding of the aorta. Electrocardiography showed left ventricular hypertrophy Erythrocyte-sedimentation rat (E.S.R.) 13 mm in one hour Hb 98%; white-cell coun 14 000 per c mm.; blood urea 67 mg per 100 ml. urinar urea 3 4 g per 100 ml Straight radiography of the abdome showed no gall stones. Serum and urinary amylase level were normal.

Treatment and Progress

Treatment with hexamethonium was begun immediatel (within an hour of admission and thirteen hours from th onset) Hexamethonium bromide 25 mg subcutaneously reduced the blood pressure to 135/80 mm. Hg By the nex day the pain had lessened and a thrill was felt over th right femoral artery The power and temperature in bot limbs were equal The blood pressure was maintained a 100–170 mm. Hg systolic and 70–100 mm. Hg diastolic b injections of hexamethonium given as indicated by the hourl blood pressure chart usually every four hours. The patien was propped up on pillows and the head of the bed was raise on blocks. With increasing tolerance the successive dose of hexamethonium were gradually increased over eigh days to 100 mg but thereafter no further increase wa necessary

Some pain in the back persisted for several days. It wa noticed that the patient complained of pain chiefly whe her blood pressure was highest and another injection wa due Injection of the hexamethonium then appeared t relieve it When unknown to the patient saline solutio was substituted for hexamethonium injections did not brin relief When hexamethonium was renewed and the blood pressure fell pain was again relieved After two weeks the pain disappeared and did not recur even when hexamethonium was temporarily discontinued and the blood pressure was allowed to rise to 220/130 mm. Hg

At this time the patient developed a new murmur—a loud continuous machinery like sound, best heard down the left border of the sternum but audible all over the præcordium and occupying the whole of the cardiac cycle with an accentuation at the beginning of systole

The E.S.R. rose to 50 mm. in one hour two days after admission The blood urea level gradually fell to 30 mg per 100 ml. Urinary output remained satisfactory and after the first day there was never more than a trace of albumin in the urine. She developed cystitis, which she said she had often had in the past *Escherichia coli* was cultured from the urine and treatment with sulphonamide was begun. The urinary infection recurred when chemotherapy was stopped but was suppressed by its resumption. Throughout her stay in hospital she had slight fever her temperature being 98°–100°F The E.S.R. remained high, and she had a persistent slight leucocytosis.

Outcome

After five weeks she was allowed up and after ten weeks she returned home The physical signs on discharge had not changed. The patient had learnt to give herself hexamethonium injections; but, with clinical recovery the interval between doses had been increased to eight hours, and with the increasing assumption of the erect posture the dose had been reduced to 50 mg On discharge the patient had no complaints and said that she felt perfectly well. When seen as an outpatient seven months later she reported that she could do light housework and had no complaints. The physical signs were unaltered.

DISCUSSION

Dissecting aneurysm of the aorta is a not uncommon post-mortem finding being found in 0 2–1 5% of cases (Lawson 1952 Mote and Carr 1942) but it is less frequently diagnosed during life, and recovery is uncommon. That some patients have recovered from a dissecting aneurysm is shown by the occasional necropsy finding of a healed dissection or of a double aorta.

Most patients with dissecting aneurysm have a high blood pressure, and this is often maintained after the onset of the dissection (Baer and Goldburgh 1948, David et al. 1947)

Figures for the time of survival after dissection suggest that more than half the patients live for twenty four hours or longer, and about 10% live for some months or years (Lawson 1952, Levinson et al 1950) In a first attack death is nearly always due to external rupture of the aneurysm (David et al 1947), but of Shennan's (1934) 79 cases of old "healed" dissecting aneurysm death was due to recurrent or second dissection with hæmorrhage in only 28 Shennan concluded

> "The main factor determining the length of survival of all cases of dissecting aneurysm subsequent to the occurrence of the primary tear is the varying period during which the blood pressure is maintained at the height at which the primary rupture has been produced"

In the present case treatment with hexamethonium was started as soon as a dissecting aneurysm had been diagnosed, and the blood-pressure was continuously maintained at relatively low levels There were no apparent ill effects from this It is impossible to say how much, if at all, hexamethonium contributed to the patient's recovery, but this treatment seems worth using in future in those patients with dissecting aneurysm of the aorta whose blood-pressures are high and who survive long enough to reach hospital

SUMMARY

A case of dissecting aneurysm of the aorta wi hypertension is described in which hexamethoniu bromide was administered and the patient recovered.

Since death in a first attack is nearly always due external rupture, it may be worth trying hexamethoniu treatment in cases where the patient is hypertensi (as he frequently is) and survives long enough to rea hospital

I am grateful to Dr A M Cooke for permission to publi this case and for his advice

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Preliminary Communication

ISOLATION OF A CRYSTALLINE PROTEIN FROM HIGHLY PURIFIED DIPHTHERIA TOXIN

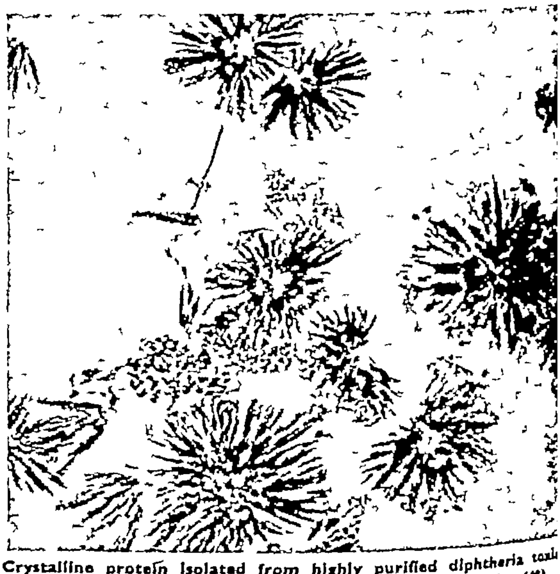
A RECENT annotation[1] in this journal reviewed progress towards the isolation of pure antitoxin The purification of diphtheria toxin appeared to have been achieved as a result of the work of Eaton[2] and Pappenheimer[3] but later work by Pope, Stevens, Caspary, and Fenton[4] suggested that the highly purified toxin still contained a large number of antigens Results supporting this conclusion were also obtained by Lepow and Pillemer[5] In recent (unpublished) work we have been able to show by electrophoretic methods that it is possible to separate these other antigens and to obtain a product which gives a single line in the diffusion test described by Pope et al[4] Unfortunately the amounts of material obtained in this way are small and this has hampered our work.

Recently we have isolated a crystalline protein from diphtheria toxin after its preliminary purification by a new method (Pope and Stevens, unpublished data) A single crystallisation yields material which shows multiple diffusion lines, but the number of antigens present has been reduced After three crystallisations a product was obtained which gave a single diffusion line in the diffusion test as usually carried out, but showed slight traces of contamination on a more prolonged test

Contamination of the crystals with amorphous material has been a big difficulty, but the thrice crystallised product appeared to be free from amorphous material Whenever amorphous material has been present on microscopic examination, multiple lines due to the presence of other antigens have always appeared

Examination of the crystalline material by in-vivo and in-vitro methods has shown a very close agreement between the values per ml calculated from these tests Preliminary results indicate that this crystalline material has a purity, in terms of *Lf*/mg nitrogen, about 50% greater than the value deduced by Pappenheimer and Robinson[6] from a study of the toxin antitoxin flocc precipitates, or the value obtained by Pappenheime on isolated toxin

While it is tempting to consider that this crystalli material is the specific toxin produced by *Corynebacteriu* *diphtheriæ*, certain anomalous results with differe antitoxins suggest that it would be unwise to consid this as more than another step towards the isolation of th specific toxin



Crystalline protein isolated from highly purified diphtheria toxi First crystallisation showing some amorphous material (× 440).

The accompanying photograph shows once crystallis material, together with associated amorphous materi obtained from a toxin having an initial purity of th order of 2600 *Lf*/mg nitrogen

Full details of the methods used for initial purificatio of the toxin and its subsequent crystallisation will b published elsewhere

C G POPE
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MURIEL F STEVENS
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The Wellcome Research
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Medical Societies

ROYAL SOCIETY OF MEDICINE

Rest or Activity?

On Nov 24 the section of medicine met, under the chairmanship of Sir HENRY COHEN president of the section to discuss the Use and Abuse of Rest as a Therapeutic Measure.

Dr G E BEAUMONT declared himself a firm believer in the value of rest. Tranquillity was necessary for cure, and bed meant a mind dulled and free from thought A patient who had been in bed for only a few days often grumbled a long stay patient was silent, because his mind was at rest. The temperatures of tuberculous patients often rose after they had been disturbed by visitors. Rest was a well known ingredient of the treatment of poliomyelitis and of pulmonary tuberculosis, and he was not sure that surgeons did right in insisting on exercises to promote lung expansion and prevent deformity immediately after thoracoplasty More lung was always diseased than was apparent from X ray examination, and quiescent foci might be activated by such therapeutic gymnastics and account for some of the present failures of cure Sciatica used to be treated with active physiotherapy until the prolapsed intervertebral disc was recognised and rest came into its own Subdeltoid bursitis was sometimes treated with movement to prevent adhesions forming," but in Dr Beaumont's view rest and deep X ray therapy was the only correct treatment As for rheumatoid arthritis, the essential was up to eighteen months in bed, with splints applied to the limbs. Moreover Dr Beaumont observed, exercise and worry were said to lead to obesity, so the way to slim was to go to bed.

On the other hand Prof W MELVILLE ARNOTT thought that rest in bed was very far from being a panacea, it was more like a drug of addiction? with some definite indications but toxic in overdoses and even fatal on occasion To put to bed was far too often the physician's automatic reaction when presented with illness. An experimental study was cited in which healthy young adults were immobilised for six weeks During this period their nitrogen balance was negative by 54 g they lost anything from 9 to 24 g of calcium, and this, with a high phosphate excretion predisposed to urinary calculi. Blood volume decreased and vasomotor control weakened, so that fainting was more common in the erect posture. It took these people six weeks to recover to normal. In old patients, it was already well known that a long stay in bed led to skeletal changes urinary calculi, muscular contractures, weakening and stretching of ligaments, bed sores, anorexia and constipation and a urinary incontinence which would often abate if the patient were only allowed up again Bed rest in many diseases was anatomically physiologically and psychologically indefensible; and 18th century physicians, such as Withering Heberden, and Stokes, did not advocate it. It was Hilton's mid 19th-century classic *Rest and Pain* which, rightly pouring scorn on the treatments of the time, had exalted rest above all. But things had now gone too far the other way especially when hospital care had displaced home care for patients in British hospitals were expected to stay in bed and the nursing was based on this. In Continental clinics and tropical hospitals the patients were allowed up much more, without detriment.

Professor Arnott pointed out that rest had many meanings one was absence from work. There was no conclusive evidence that hard work ever caused illness: rather the reverse. The industrial 40 hour week was an economic and political concept, not a medical one But a diagnosis of overwork hid the doctor's ignorance of ætiology and pleased the patient by depic him as a martyr before his family and friends physician had a duty to prescribe absence from w very carefully not merely in the patient's own inte but for the economic health of the country

Prof C A WELLS said he had found Hilton's book q unreadable It was irrelevant to modern surgery, wl set out to modify nature profoundly Sympathecto for example, was used to relieve the pain of an pectoris and permit a patient greater activity how t could previous pain have been a true indication for re The resting of a part was still useful in the treatmen bone and joint tuberculosis, but this did not m immobilising the whole patient; indeed, in ort pædics, muscular activity inside a plaster was axioma At Leysin, Rollier was going even further and treat *spinal* caries without plaster at all the children me lay face down in the sun and encouraged their erect spinæ muscles to develop and steady the disea vertebræ Professor Wells advocated the same techn for the prevention of prolapse of an intervertebral d In a different field a patient with severe bedsores l been saved by being turned from side to side hou day and night for rest would have been fatal

After every surgical operation, deep venous thromb was one of the risks of resting in bed—a risk grea increased if Fowler's position were still used In Profes Wells's wards every patient did a daily ten minutes leg and deep breathing exercises starting on the v day of operation, and everyone had to start getting of bed within forty-eight hours. In Madrid he l seen a partial gastrectomy performed under lo analgesia on a man who at the end got up, put on shirt, and walked back to the ward where he v forbidden to get into bed. Early ambulation was new thing Professor Wells read part of an account an ovariotomy performed in 1809 without anæsthe or asepsis, where the surgeon found the patient up a making her own bed on the fourth postoperative d Finally as another example of a new technique maki nonsense of old ideas, he instanced hibernation Bef anæsthesia began the patient was given chlorpromaz hydrochloride which inhibited the temperature cent of his brain and allowed his body to be cooled to rectal temperature of 30 C for the period of the operati without harm to brain or kidney Less anæsthetic a less oxygen were needed during the operation and all t manifestations of 'shock' were diminished Th temporary unphysiological resting of the patien tissues earned quicker recovery later with amnesia f the whole treatment.

Group Captain C J S O'MALLEY as an authori on rehabilitation, took a middle line, and quoted t R.A.F rehabilitation couplet Intermittent rest an work makes a strong and healthy erk ' He instanc the treatment of acute poliomyelitis, where he agre with Seddon that a policy of graduated exercises ga better results than either immobilisation or exerci to fatigue. He had seen improvement as late as thr years after infection when the patient took his exercis with the will to get better The problem was to kno how long to rest and when to start activity Formerl after meniscectomy for internal derangement of th knee a patient was still not back at work after twel weeks. In the R.A.F such cases went to a rehabilitati centre two weeks after operation and were back at wor in six to eight weeks. Now at Garston Manor case arrived three to five days after operation and the were back at work within four weeks. A similar speed u in recovery had taken place with herniotomies th was achieved by courses of exercises, morning and afte noon divided into half hourly periods each of whic ended with ten minutes rest and by games and wor therapy to encourage unconscious movements. Asthmati and bronchitis could be greatly helped by these courses, and they were also valuable for patients with neurosis During the war, Group-Captain O'Malley had treated orthopædic and psychiatric patients together—in the proportion of four to one In the rehabilitation centre patients got away from the hospital atmosphere of disability Such centres were cheaper to run than hospitals his own cost £7 7s 6d per occupied bed per week, whereas, on the same basis, a hospital was two to four times as expensive It was a pity that convalescent homes did not recognise these methods of rehabilitation He was convinced that rest was an overworked treatment, and he cited recent observations that in osteo arthritis of the hip it was daily use which preserved the articular cartilage He thought it significant that opposition of finger and thumb was one of the last movements to go in rheumatoid arthritis—because it was in daily use

During the discussion, Dr F H STEVENS asked for medical research into the gross osteoporosis which takes place when prolonged rest is inevitable, and Dr J W TODD wanted the Medical Research Council to undertake controlled clinical trials of rest therapy The PRESIDENT pointed out that there was some semantic confusion over the meaning of rest, and that it was unwise to make wide generalisations The treatment of coronary infarction or peptic ulcer, for instance, was bound to vary according to the extent of the lesion, the nature of the patient, and so on, and universal legislation was impossible

Reviews of Books

Basic Pathology and Morbid Histology

D B CATER, M A, M D Camb, F R C S, University demonstrator in pathology, University of Cambridge Bristol John Wright 1953 Pp 320 42s

Dr Cater's commendable aim has been to bridge the gap between physiology and pathology for the student, and to help him to understand his earliest lessons in pathology at a time when his knowledge of clinical medicine is necessarily scanty He strives to "graft on to the student's knowledge of physiology sufficient clinical information to make pathology live." By producing an easily read and graphic account of the basic pathological processes, with interesting historical references, and by making effective use of analogies between disease and warfare, he has succeeded well in his purpose But though this volume deals with basic pathology it is more than elementary the student, when he has assimilated its contents, will be equipped with up-to-date knowledge of many of the engaging problems of pathology, as well as with the essential established facts Camera-lucida drawings, several of which are in colour, are used abundantly and with effect · being admirably clear they are to be preferred to photomicrographs in a book of this kind The author and his wife evidently spent a great deal of time on their careful preparation

Pituitary Chromophobe Adenomas

Neurology Metabolism Therapy JOHN I NURNBERGER, M.D, research associate, Institute of Living, Yale University School of Medicine, SAUL R KOREY, M.D, associate professor of neurology, School of Medicine, Western Reserve University New York and London Springer 1953 Pp 282 £2 15s

THE experiences and even the fate of a patient with a chromophobe adenoma of the pituitary may differ greatly according to whether chance puts him into the hands of a general physician, a neurologist, or a "metabolician" Consultation between specialists is not always as helpful as might be hoped, because they may not speak the same language, the neurologist, for instance may not always be familiar with the biochemical terms which describe the metabolic disorders of patients with pituitary tumours Yet the patient must surely benefit if a broad view can be taken of his illness In this book two neurologists who [illegible] equipped to discuss pathological and biochemical problems have set out to "correlate information from several medical disciplines in order to portray the syndrome of chromophobe adenoma of the pituitary in its setting of pathologically modified function"

They analyse the records of 117 patients with this condition who were admitted to the Neurological Institute of New York or to the Medical Service at the Presbyterian Hospital between 1929 and 1948, and who were investigated from the neurological and metabolic standpoints. They provide a fairly comprehensive review of their subject with more than 500 references The book is long for its purpose, and the style suffers from the Germanic defects of American medical writings Fortunately, the layout makes up for such defects and the essence of the material is available in summaries which provide frequent resting-points

The fragmentation of medicine into specialties is creating a problem for our schools and teachers of medicine Not only neurologists and endocrinologists, but also the diminishing band of general physicians must welcome a book like this, which brings together two separate disciplines

Classics in Clinical Dermatology

WALTER B SHELLEY, M.D, PH.D, chief, clinic of dermatology, University of Pennsylvania Hospital, JOHN T CRISSEY, M.D, instructor, dermatology and syphilology, University of Pennsylvania Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications. 1953 Pp 467 75s 6d

THESE authors have brought together the original versions or careful English translations of 143 classical descriptions of skin diseases, by 95 writers The diseases depicted vary from the commonplace to the very rare Some accounts are individual case-reports, while others are the results of the prolonged study of many patients.

The writings are arranged chronologically, and contributions vary in length from 1 to 15 pages, von Hebra and Brocq being allotted the largest space Robert Willan (1757-1812) has pride of place as the father of modern dermatology, whose classification, based on morphology, reads almost as well today as it did when it was written his pupil Bateman (1728-1821) produced the first atlas of dermatology Among the other great names of dermatology included are Alibert Cazenave, Bazin, von Hebra, Erasmus Wilson and Tilbury Fox, Jonathan Hutchinson and Radcliffe Crocker, Pringle, Unna, Besnier—with extracts from their most important contributions Excellent reproductions of original illustrations to the articles are scattered through the clear and pleasingly displayed text

This delightful book will please all interested in the history of medicine and in the eponymous figures of dermatology

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Parsons' Diseases of the Eye (12th ed. London J & A. Churchill 1953 Pp 606 42s)—The task of revising this favourite text for its twelfth appearance has been committed to Sir Stewart Duke Elder In the preface Sir John Herbert Parsons joins him in saying how thorough, in view of modern advances, this revision has had to be indeed, the whole text has been reset Fortunately the anatomy of the eye has remained much the same, though the physiology has displayed some of its well known restlessness Our knowledge of the ætiology and pathology of ocular diseases has advanced very fast, and, though rare diseases continue to be refused admittance, room has had to be made for such conditions as toxoplasmosis and retrolental fibroplasia which have established their importance in ocular pathology But, as every preface to a textbook on disease nowadays exclaims, the greatest changes have been in therapeutics, and in the field of ophthalmic surgery there is also much to be said about new anæsthetics The result of these upheavals is a virtually new 'Parsons" not only up to date and better illustrated, but—mirabile dictu—slimmer

Textbook of Bacteriology (7th ed London Heinemann Medical Books 1953 Pp 492 20s)—Dr R W Fairbrother's popular book is back again in a new edition, a little (but not much) stouter as age advances With revision some parts have been reduced in size, and in particular, the sections dealing with bacterial metabolism, chemotherapy, and the viruses have been brought up to date

THE LANCET

LONDON SATURDAY DEC 5 1953

More Beds?

THE last five years have seen many improvements in our hospitals Wards that were grossly over crowded have had their beds reduced to manageable numbers, nursing arrangements have been modernised, and a great deal has been done to brighten up the appearance not only of wards but also of corridors and special departments At the same time there has been much skilful and relatively inexpensive reconstruction of hospital buildings to provide better quarters for outpatients, for special departments, and for resident staff

When the hospitals were taken over by the National Health Service, between 10% and 15% of their total complement of beds were no longer in use—chiefly because of the war and its consequences. But this original complement included much unsatisfactory and overcrowded accommodation, and the time has come when these pre-war figures should be forgotten and the development of the hospital services should be considered only in terms of staffed beds In the Oxford region for example, we find that better spacing, better sanitary arrangements, and the abandonment of unsuitable premises have meant a loss of 116 beds belonging to the former complement, but despite this loss the management committees have 440 more beds at their disposal.[1] In England and Wales in 1952 463,255 N.H.S hospital beds were available for patients—an increase of some 20 000 since 1949[2] This increase has been obtained almost entirely by reopening closed wards and by using beds formerly kept vacant for infectious diseases and most of the extra beds have been allocated to the chronic sick and to specialties such as gynæcology ear, nose, and throat surgery, traumatic and orthopædic surgery and chest diseases. Perhaps more important however, than the increase of staffed beds has been the increase in the turnover of patients. In England and Wales the number of discharges per bed for general medicine rose from 11 6 in 1950 to 13 1 in 1952, and similar increases took place in other specialties Regionally the biggest increase has been that achieved by the Newcastle board, which between 1950 and 1952 improved its turnover by 16 2%[2] The improved supply has liberated an increased demand, and the pressure on hospital beds remains very great but it nevertheless looks as though the problem of hospital accommodation can be solved within a reasonable time and without astronomical expenditure The present situation is well set out by Dr F N MARSHALL, S A M.O of the Manchester Regional Hospital Board[3]

> Once again the picture presented by the returns for the year 1952 is encouraging Although the amount allowed to the Board for capital projects is barely sufficient to keep existing buildings in a proper state of repair and certainly inadequate to allow large scale building operations to be undertaken it is gradually becoming evident that, except for mental and mental deficiency purposes not many more beds are required to enable an adequate service to be given. That is not to say of course, that the quality of the hospitals and beds is satisfactory or that in certain areas there is not a definite shortage of first-class beds. Nor does it imply that hospital management could not be facilitated or that great savings could not be made in maintenance costs if some of the smaller buildings could be replaced by extensions to central or base hospitals. The returns do show however that following the redistribution of the specialist staff, the tightening up of the management consequent upon the grouping of hospitals and the abolition of outmoded rivalries, the provision of better equipment, operating theatres, laboratories, X ray departments physiotherapy and out-patient facilities, etc., the turnover in existing in patient beds has been much improved. In 1950, for instance, the number of in patients discharged from or died in the Board s hospitals was 203,414 In the same hospitals the corresponding number for 1952 was 280,593—an increase of over 10 per cent. In the same period new out-patients increased from 460 501 to 490 828 Further improvements are still possible, provided adequate nursing domestic and medical staff can be obtained but it is becoming increasingly obvious that there is a limit to the number of persons the country can spare for hospital duties and, to make the best use of the personnel available, capital investment will be necessary to concentrate their efforts and to avoid dissipation of their energies. This redistribution and building up of the specialist services is undoubtedly the most valuable service the Board has yet performed in the interests of the community it serves.'

This is, we fancy, the first post war occasion when anyone has publicly stated that there are nearly enough medical beds in any region It has however, been well recognised that the pressure on children's *beds has been much reduced and that many pædiatric* units are not always filled.

For mental hospitals and mental-defective colonies the position is far less satisfactory as was emphasised in last month's debate in the House of Commons.[4] In mental hospitals gross overcrowding still exists and it is officially estimated that mental hospitals and institutions contain 14 7% more patients than they properly have room for This overcrowding is of course worse in some of them than in others, and what it can mean in actual physical conditions was vividly brought out in the debate by Miss ALICE BACON Commenting on one mental hospital in the Midlands she said

> The wards have to be seen to be believed I saw a ward, about the size of a normal hospital ward which contained 112 beds for female patients There was not sufficient room for the patients to undress inside the ward. They had to undress in another room which, in the daytime was used as a recreation room I was curious to know how the 112 female patients managed to find their own clothes in the morning, when they were left on the floor of the recreation room at night. I was told that the female patients had their names stitched inside their corsets. Their clothes were then rolled up inside their

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[1] The Hospital and Specialist Services, Oxford Regional Hospital Board, 1953.

[2] Report of the Ministry of Health for 1952. H.M. Stationery Office 1953.

[3] Report of the Manchester Regional Hospital Board for 1952.

[4] Hansard 1953 520 no. 8 (Nov 12) See *Lancet* Nov 21 p 1091

corsets and put on the floor at night, in 112 bundles, and the patients had to be filed into the wards where they slept and filed out again in the morning to dress "

The position of institutions for mental defectives is if anything even worse, and the waiting-lists rose from 5316 in 1949 to 9300 in 1952 The worse the living conditions become, the harder it is to retain staff, and an acceleration of the present programme for improving these conditions is desperately needed Present plans provide only for 3000 additional beds for mental defectives and about 1500 further beds in mental hospitals within the next five years

What has so far been done has been done with relatively little capital expenditure One of the lessons we have learnt is that very often an old hospital ward can be modernised at a small fraction of the cost of building a new one—as witness the new professorial unit of Maryfield Hospital, Dundee In the five years under the N H S , £35 million has been allocated to capital works[2]—mainly war-damage repairs, minor reconstructions, and major items of repair and replacement—and this may be roughly compared with the amount spent on new schools, which was £96 million in 1948–52[5] Although the picture for general hospitals is on the whole encouraging, perhaps twice the sum so far provided for capital expenditure will be needed over the next five years to complete the process of modernising old buildings There is also urgent need of a limited number of major hospital schemes to equate hospital beds with local increases in population, for virtually no hospital provision has yet been made for new towns Furthermore, the time is ripe for the rebuilding, and in some cases the re-siting, of several of the teaching hospitals So far, the teaching centres have been able to do little more than stand still, while the hospital services elsewhere have been improved The needs of medical science, as well as the reputation of British medicine overseas, make it increasingly necessary that our teaching centres should be able to hold their own architecturally with hospitals elsewhere in the world

Peripheral Embolism

A QUARTER of a century ago, surgeons boldly took up the challenge of peripheral arterial embolism, with its dramatic onset and often disastrous consequences embolectomy seemed the only means of saving limb and often life **SSABANEJEFF**[6] is credited with the first attempt at this operation in 1895, and **LABEY**[7] with the first successful operation in 1911, this was at a time when the sequelæ of chronic peripheral arterial disease, except for aneurysms, were thought to be beyond the scope of the surgeon, who had the humble rôle of amputationist after gangrene had supervened During the past twenty-five years, thanks largely to the vision and pertinacity of **LERICHE**, surgery has come to play an increasingly important part in the treatment of chronic ischæmia of the limbs, with operations to interrupt the sympathetic pathway, and to restore the blood-flow through obstructed arteries by " disobliteration " or grafting Rather surprisingly this period of great expansion and technical progress in vascular surgery has coincided with an increasing reluctance to resort to operative removal of arterial emboli Brilliant results from operation have been offset by many disappointments, owing to precarious cardiac condition of the patients, multiple or recurrent emboli, and, most often, too tardy intervention Clearly the retreat from the policy of a generation ago has corresponded with the introduction of anticoagulants. Armed with these drugs, physicians, who see most of the cases of embolism, have observed more attentively the natural course of events, and have been impressed by the survival of many limbs—and patients—without surgical treatment Prominent among the factors influencing the outcome in untreated cases is the site of the embolus It has long been recognised that in the upper limb gangrene rarely ensues and recovery is usually unattended by appreciable functional impairment In the lower limb, emboli lodging below the knee may likewise cause only transient pain and weakness On the other hand *calamitous consequences usually result from* emboli lodging at the bifurcation of the aorta or in the iliac arteries, and often from femoral or popliteal emboli In the great majority of cases embolism arises from rheumatic heart disease with auricular fibrillation, or from arteriosclerosis with coronary thrombosis and cardiac infarction , and the prognosis depends largely on the cause **ANDRUS**,[8] describing a series of 57 cases treated without operation, says

> " In general, it may be said that the patient with arteriosclerotic heart disease has a much poorer prognosis because of the severity of the cardiac lesion itself and the lack of cardiac reserve, in contrast to the patient with uncomplicated rheumatic heart disease, who, despite the presence of fibrillation and the development of a clot in an auricular appendage, often has a fairly good cardiac status In addition, the peripheral arterial system in the rheumatic patient is ordinarily normal because of his lower age and the fact that the disease is usually limited to the heart itself In the elderly patient with arteriosclerotic heart disease, however, the process which has affected the myocardial vessels usually represents only a part of a widespread disease and has brought about a serious narrowing of the peripheral vessels as well "

Initially spasm of the arterial wall occurs at the site of the embolus and to a varying extent distally, and this may itself impede the development of collateral circulation and endanger the limb After a few hours secondary thrombosis, spreading mainly distally from the embolus, further reduces the blood supply by blocking the mouths of available collateral arteries Thus the promptness with which operation is done is most important In cases which are not operated on, the course is largely unpredictable, for proneness to vascular spasm and to thrombosis varies widely between different people and in the same person according to his health and physiological activity Spasm can now be combated with procaine and other antispasmodics administered by paravertebral sympathetic infiltration or by intra-arterial injection, and thrombosis by anticoagulants, the most important of which is heparin Yet **ANDRUS**,[8] reviewing cases treated with anticoagulants and antispasmodics without embolectomy, states

> " it must be admitted that almost all patients who had suffered embolism of the leg vessels and survived without gangrene had some impairment of function or

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[5] Ministry of Education Education in 1952

[6] Ssabanejeff *Russk Khir Arkh* 1895 11, 625

[7] Labey *Bull Acad Méd Paris*, 1911, 66 358

[8] Andrus W De W *Arch. Surg* 1950, 60, 511

limb Their disability varied from mild weakness signs of circulatory deficiency such as intermittent dication to severe weakness and neurologic disturb es such as numbness, tingling or spontaneous pain the involved extremity In the elderly arteriosclerotic ent this, while not ideal, presented a tolerable dition, but in a number of younger patients it con uted a serious handicap to an active life.

DRUS concludes that in patients seen less than elve hours after the onset of femoral or popliteal bolism secondary to rheumatic heart-disease with t cardiac decompensation, the addition of emboleo ny to conservative measures would improve the rly results and avert much of the late disability holds that embolectomy is imperative for all tients with saddle emboli of the aortic bifurcation, emboli in the iliac arteries, who will tolerate the eration. At present arterial embolism should *ways be regarded as a potential surgical emergency* d the patient should immediately be placed under nditions where prompt operation is possible RTY[6] writes thus

> “Decision is the keynote of success in the management peripheral emboli Preparations must be made for eration at the earliest possible moment. Temporizing easures should only be considered when the cardiac ate of the patient absolutely contraindicates operation a rare contingency *when it is remembered that most* bolectomies can be performed under local anaesthesia. the interval between the onset of symptoms and eration all possible measures should be employed to omote the collateral circulation and to delay throm sis. Occasionally such an improvement in the circula on of the limb will follow sympathetic block and dministration of heparin that postponement of operation ill be justified Only recovery of such degree that the eripheral pulses re-appear can justify persistence with n-operative measures beyond 8 or 10 hours After is interval embolectomy is menaced by rapidly iminishing chances of success, but with the use of eparin and sympathetic block the period for possible ccesses may come to be appreciably extended. When xploration reveals adherence of the embolus, secondary hrombosis or a damaged arterial lining arteriectomy nd perhaps disobliterative endarteriectomy offers the est hopes of conserving limb function and life

Further improvement of medical or surgical treatment may finally *bring embolism decisively within* the orbit either of the physician or of the surgeon or perhaps a more discriminating appreciation of the needs of each patient may bring both together with better results than either can obtain alone Meanwhile, more data should be collected on the long term functional results in limbs which have urvived an embolus under conservative and under perative treatment

Milk and Water

THERE has long been a tenet that a mother who has insufficient milk for her baby should drink as much as she can. It is a natural enough belief, and there has seemed to be more to it than mere wishful thinking because of the misleading facts of the draught reflex. When a baby goes to the breast there is normally a centripetal nervous stimulus which evokes a humoral discharge from the posterior pituitary gland. This secretion, carried round the body, causes contraction of the myo-epithelial cells round the alveoli of the mammary gland The pressure within the breast rises sufficiently to give the mother a sudden tense feeling in the breasts and milk often runs from the nipples Many people who have to deal with lactation—farmers doctors nurses, and mothers—have difficulty in believing that this is not the time when the milk is made in fact, it is made at an almost constant rate day and night The draught reflex is the essential part of the mechanism of milk withdrawal This reflex, evoked primarily by the baby taking the breast, can also be set off, when the breasts are full, by the mother thinking about her baby or performing actions associated with feeding time Many women who make a habit of drinking water immediately before a feed experience the draught reflex on taking any cold drink This is the misleading fact, for as the mother puts the glass down she feels the “milk coming into her breasts” and may see it flowing out, so she naturally concludes that she has been making some extra milk Successful lactation requires an effective and appropriately timed draught reflex and research has shown that the reflex should not be falsely evoked In the cow the corresponding reflex, when elicited, must be followed by milking at exactly the right time or the milk yield is reduced, and it cannot be so effectively evoked a second time In the human the draught is more vigorous when the *child takes the first breast than when he takes the* second, and presumably it cannot be constantly repeated A draught reflex evoked by a cold drink may therefore expend the vigour that should have been saved for the baby when he takes the first side

The false evoking of the draught reflex, which is probably the basis of the hydration treatment of deficient milk secretion, may thus be an actual hindrance to lactation. Moreover, as GUNTHER has lately pointed out[1] the flooding of the body with water is likely, on its own account, to antagonise the draught reflex CROSS[2] has shown that the draught is accompanied by another posterior pituitary effect—the antidiuretic action. If diuresis has been forced on the body by water drinking the secretion of the posterior pituitary antidiuretic substance must be impaired, even though its accompanying effect of *producing contraction of the myoepithelial cells would* be appropriate

Despite these physiological considerations, the custom prevails of persuading mothers to drink large volumes of fluid Six pints of water in addition to tea, coffee cocoa, milk and soup is not an unusual daily amount Some mothers complain that they are sick of water, and all who are taking these large quantities of fluid find frequency troublesome even when they are up and about and do not have to wait for a bedpan They will therefore be grateful to Professor ILLINGWORTH and Dr KILPATRICK who in an investigation described in this issue, have demonstrated that lactation is hindered rather than helped by much drinking They found that mothers who drank only as much fluid as they felt inclined were able to give more milk on the ninth day after delivery *than a comparable group of women who* deliberately took nearly six pints a day Those who were left to their own inclination took an average of about three and a half pints daily So we would be wiser and kinder to offer, rather than prescribe fluids at the time of lactation.

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[6] Harty F *Postgrad. med. J* 1951 27 117

[1] Gunther M. *Univ Coll. Hosp. Mag., Lond* 1953, 38 82.

[2] Cross, B A. *J Physiol.* 1951 114, 447

Annotations

CHOOSING UNDERGRADUATES

RACE HORSES, uncertain, coy, and hard to please, are notoriously rough on the prophets, but compared with entrants to university education they are models of predictability Those who have to assess, in advance and on short acquaintance, the likely performance of a horde of young persons wearing the muffin-like mask of adolescence, are confident—like other followers of form—of their flair for picking winners

But such evidence as we possess by no means fully justifies their faith in themselves According to a new P E P broadsheet,[1] few studies have been made of the causes of failure of students (defined, that is, in terms of failure to get a degree), but at a conference of the Home Universities last year Sir Alexander Carr Saunders gave some results of an analysis made at the London School of Economics

> In 1949, 305 full time students were admitted to the school to read for the degree of B SC (Econ) All should have taken the degree in 1952, but only 207 did so Of the 98 who did not, however, 33 were not 'failures "—they transferred to other courses or withdrew for personal reasons The remaining 65 failed at examinations at the end of their first, second, or third year Only 1 did, in fact, fail in the third year, at the final examination The interesting thing, however, is that, at entrance, 27 (41%) of the 65 failures were considered to be first class, and 31 to be good, the remaining 7 were thought to be adequate

A parallel study was made by the Working Party on University Awards,[2] who found that of the undergraduates of one university who took good degrees (firsts or good seconds) from 1935 to 1941, 46% would not have qualified for awards on their marks in the Higher Certificate examination

At the moment, there are available every year 2000 State scholarships (including 30 scholarships for mature students and 120 technical scholarships) The Ministry of Education have undertaken to supplement up to 2000 open university scholarships of an annual value of £40 or more, and so far there are 1400 of these In addition, there are 8800 major awards by local education authorities Of the 22,000 undergraduates entering universities in 1951–52, over 15,000 were assisted with public funds from one or other of these sources The idea is that the university awards supplemented by the Ministry should go to outstanding students, selected by competitive examination, while the local authority awards should provide for the good average student Each of the 146 local education authorities decides the number of its awards, their value, and the conditions on which they are made, but only 40% of the money comes from local rates—the rest is provided by the Government When it comes to deciding who is to have awards, the universities not unnaturally think that they should pick their own entrants, and that any young person who, in their opinion, is good enough to be offered a university place is also good enough to be offered a local authority award—which, indeed, should come to him as a matter of course The local authorities not unnaturally think that as they are providing nearly half the money for their awards they should have the right to say who will get them Many make an award conditional on the candidate's getting a university place, but it is not unknown (though it is unusual) for a student who has been accepted by a university to be subsequently refused an award by the local authority Moreover, according to the local authorities, the universities are not necessarily the best pickers P E P quote a correspondent

> 'Local authorities are noticing an increasing number of rejects after the first year in a university Every reject means that anything between £150 and £250 has, so to speak, been thrown out of the window In fact some local education authorities have doubts (and some of them considerable doubts) about the selection procedure of some universities"

Generally speaking the universities base their decisions on the young person's school examination performance, supplemented in some cases by his success in a college entrance examination, on his school record and testimonials, and usually on an interview Some of the larger universities do not attempt to interview all candidates, the numbers seen range from 10% to 80% Those universities which use the interview for all candidates prize it highly as a selection procedure The universities themselves are the first to admit that existing entrance tests do not measure the candidate's power of adapting himself to a new environment, a new approach to subjects, a different method of study, and the other changes implied in the transition from school to university And again, what is success? Is the final examination of the university a good enough criterion? P E P quote a statement by the Civil Service Selection Board that the 100 candidates whom the board placed at the bottom of the 3000 they examined over a period of three years included 60 who had been university or college scholars, 20 who had held State or county scholarships, and 10 who had first class degrees It seems that the criteria applied in the university do not necessarily overlap with those applied elsewhere

In this puzzling situation P E P come to the conclusion—in some ways unexpected—that responsibility for selection should rest solely with the universities, and that the granting of an award should automatically follow the acceptance of a student by a university This could be arranged, they suggest—and no doubt they are right—if the Government assumed full financial responsibility for all awards and not merely for 60% of their cost, as at present All candidates, they say, would then have at least an equal chance of being considered for a place They also think there might be a more liberal policy of admissions to the university followed by a more rigorous weeding out at the end of the first year, when those unlikely to complete the course are more easily detected (The effect of such a measure on the suicide rate among undergraduates is a matter for speculation it might, of course, reduce it) But even if the grumbles of the local education authorities were thus effectually silenced, the general public would surely deserve some assurance that the best boys and girls were getting the awards, and that money was not being wasted The universities recognise that their methods of selection fail to take into account some of the qualities which go to make a good student, and research on selection problems is now in progress When the results of the Nuffield Foundation and Medical Research Council inquiries are published they will no doubt influence not only techniques of selection but also the content of university courses, and methods of teaching We must not, however, expect miracles, even then it is most unlikely, as P E P are careful to point out, that these findings will produce "a single compendious test which, applied at the school-leaving stage, will enable accurate forecasts of performance to be made"

A HAZARD OF ANÆSTHESIA

AN endotracheal tube is generally regarded as a certain safeguard against the possibility of respiratory obstruction during anæsthesia Its everyday use has not only safeguarded many lives, but has made many operations incomparably easier—particularly those on the head and neck Even an endotracheal tube, however, may be kinked, or, as in a recently reported fatal case,[1] obstructed by an inflated cuff Anæsthetists ho have not already given thought to this possibility hould note that an inflated cuff may block the end of n endotracheal tube if the lower edge of the cuff is ose to the end of the tube and the rubber of the cuff very thin It may also block a soft endotracheal ube by compressing the lumen of the tube Softened ubes—usually the result of long boiling and greasy ubricants—should be discarded

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[1] *Planning* 1953 19 249 Issued by Political and Economic Planning, 16, Queen Anne's Gate London S W 1
up by the Minister of Education 1948

[1] *Glasgow Evening News*, Nov 12, 1953

WHO IN AFRICA

FOLLOWING a general policy of decentralisation, W H O ransferred its African regional office from Geneva to Brazzaville in October 1952 and the director of this ffice has now reported on the first year's work [1] The ifficulties of recruiting an international administrative nd secretarial staff for work in Africa have been made worse by placing the office in one of the most expensive owns in the whole world (W H O have had to rent partments for their staff at $285 a month) the town acks a reliable supply of water and electricity, and the mall staff have had so many purely domestic problems hat it is remarkable that they have been able to get round at all Nevertheless, the director, the public health medical officer, the sanitary engineer the health nspector the nurse, and the cultural anthropologist, who comprise the main executive part of the staff have all toured widely They have started to persuade the various African governments of the advantages of coöperation in international health and have initiated local educational projects. The account suggests that the Organisation still demands from its staff some of the adventurous spirit of the nineteenth-century African pioneers.

In the second half of the report the director Lieut General F Daubenton, allows himself on retirement after three years of office, some general reflections on health work in Africa. He points out that without the help and coöperation of enlightened Africans all foreign plans must fail No large-scale plans for technical or other development in Africa should begin without profound study and research, *Festina lente* is the motto recommended for enthusiasts The African village will for a long time be the site of the most important health problems and here he quotes Dr J M Karefa Smart one of his staff

> "The sense of community is paramount. People do not live for and to themselves in the village. All ethical values derive from the demands of what is good for the community and for the most part individual goals and objectives are tolerated only if they contribute towards and do not conflict with the goals and objectives of the community as a whole Secondly an understanding of the village permits of no division of the life into separate compartments. Just as there is in the mind of the villager no interruption in the continuity of life, from the spirit world at birth back to the spirit world at death, so there is no separation of the economic or material from the spiritual components of village life All of life is one.

Thus no scheme should be started unless its purport has been thoroughly explained and the coöperation of the villages concerned effectively secured Otherwise material will be unappreciated and machines and machinery foreign to their ideas will be neglected

In Africa today it would be better to have early twentieth-century medicine widespread, rather than the most modern forms of treatment within the reach of only a few In his travels General Daubenton has seen an X ray plant where there was no reliable electricity an elaborate obstetrical table unused while the 'bearing down' rope attached to the ceiling badly needed replacement and heavy dental and other equipment imported before the local roads and bridges could support them These errors could have been avoided by more thought and less hurry Industrialisation in Africa has started and will go on Africans themselves ask for it but only a few of them may realise how industrial development will alter their philosophy, their traditions, and their social culture Undoubtedly the most important task before W H O in Africa is educational. But all forms of medical training must do more than teach techniques for new techniques will have to be integrated with a social philosophy adapted to a new Africa and acceptable to Africans

THE SEAWEED FLIES

DURING the past few weeks South Coast towns have been much troubled by a spreading plague of flies breeding on seaweed The insects have been identified as belonging to the genus cœlopa,[1] which has long been recognised along the Atlantic seaboard of Europe from Spain to Norway The fact that it has not previously made itself a nuisance explains why little is known about it other than its morphology The present invasion is a new phenomenon which started in late August and grew to much greater proportions during September and the mild weather of October The flies and their larvæ have been detected in seaweed and especially in the shingle on beaches from Dorset to Kent and they have spread to the Home Counties probably in loads of shingle carted inland as building material Attracted by certain hydrocarbon compounds, the flies have swarmed in dry-cleaning establishments, metal works, cellulose-spraying booths, and other places where organic solvents are used There is at present little evidence that they are attracted by food or refuse but it is impossible to rule out danger to the public health from this cause, for flies can change their habits.

The breeding area is that part of a shingle beach which is reached by the sea only at the highest tides in the fortnightly cycle Here below the surface of the shingle at a depth to which neither rain nor extremes of temperature can penetrate are ideal breeding conditions of saline moisture and inexhaustible quantities of macerated seaweed. The larvæ hatching from the eggs penetrate several feet into the beach, and after pupation they appear as flies, which then emigrate to the dry beach above high water mark. They seem able to complete their life-cycle in the crevices of the shingle, though warm sunshine brings them out in thousands to swarm in a frenzy a few inches above the pebbles. Sometimes they rise several feet above the beach and settle down in steady flight—always towards the east. It is this surprising habit which has led to the spread of the invasion up the channel coast.

Measures to control the plague have been hampered by lack of information about the life-cycle and habits of the fly and its larva, but energetic experiments by the health department of Brighton have yielded many useful data on the insecticides to be used and their methods of application There are two difficulties to be overcome: the rapid provision of measures to control the fly nuisance on the beaches of holiday resorts and the much greater problem of disinfestation of the tidal strip of the Channel coastline The day-to-day control of the flies in the holiday season can probably be achieved effectively enough by a suitable knock-down insecticide in the form of a fog or light spray But the clearing of some two hundred miles of coast can be quickly accomplished only if the Government takes steps to supplement and coordinate the work of the local authorities as was urged in the House of Commons last week. Coördination is necessary from the outset not only to achieve the complete success which will eliminate any reservoir of future infestation but also to ensure that the insects do not become resistant to insecticide.

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[1] Report of the Director of the Regional Office of Africa, 1953 RC3/AFR3 Obtainable from W H.O., Palais des Nations, Geneva.

[1] See *Lancet* Nov 21 1953 p 1106.

because of inadequate doses Meanwhile the Ministry of Health and local health authorities will be keeping a look out for any disagreeable moves by the flies, from the epidemiologist's point of view they seem to be remarkably well behaved at the moment

HEPATIC CIRRHOSIS AND PROSTATIC ENLARGEMENT

WHEREAS the secretion of hormones is exclusively a function of the endocrine glands, their excretion and inactivation, by which a balance is maintained, appear to be mainly controlled by the liver In the liver they are converted to inactive derivatives or to compounds more readily excreted by the kidneys than the unchanged hormones Although much of the recent work on this subject has been concerned with the steroid hormones, there is also evidence that thyroxine and the posterior pituitary antidiuretic factor also undergo at least partial inactivation in the liver In view of this extremely important hepatic function, it is not surprising that signs of endocrine disturbance are now well-recognised features of liver disease, especially of cirrhosis[1 2] These signs arise predominantly from hyperœstrogenism, and they include gynæcomastia, testicular atrophy, and loss of libido in men, and menstrual disorders and impaired fertility in women

Fortunately the results of hormonal imbalance are not always a disadvantage to the patient This is well shown by Stumpf and Wilens[3] in their study of the incidence of prostatic enlargement in portal cirrhosis Their figures were collected from necropsies on 333 patients with cirrhosis and 359 non-cirrhotic controls Both groups consisted entirely of men over 50 years old In the control group 53% had gross prostatic enlargement—a proportion that agrees well with other published data for this condition, but in the cirrhotic group only 30% had enlarged prostates If only the moderate and severe cases of enlargement are included, then the difference is even more striking—namely, 30% in the controls and 8% in those with cirrhosis—and becomes statistically significant Not only were those with cirrhosis less likely to get prostatic hypertrophy, but the figures also indicated that when the prostate did enlarge it did so later than in the controls For example, in the age group 50–69, the frequency of moderate or severe prostatic hypertrophy in men with severe cirrhosis was 6%, compared with 28% in the controls, whilst in the 70–79 age group the corresponding figures were 17% and 23% respectively Confirmation of this inverse relation between cirrhosis and prostatic enlargement is provided by the much greater incidence in the control groups of the secondary results of prostatic hypertrophy—e g, hypertrophy of the bladder (which was twice as common) and hydro-ureter (which was four times as common)

In speculating on the cause of these differences Stumpf and Wilens rightly say that "the condition is not necessarily hormonal in nature, yet the fact that œstrogens are not properly inactivated in liver disease suggests that these may be involved" It is well established experimentally that œstrogens can antagonise the stimulating effect of androgens on the prostate in castrated animals[4] Moreover, the beneficial effect of castration upon benign prostatic hypertrophy suggests that the stimulating effect of the testicular androgens is of significance in the pathogenesis If this be so, then the antagonistic effect of the hyperœstrogenism associated with cirrhosis could account for the lower incidence of prostatic hypertrophy An alternative or contributing mechanism may perhaps be related to the fall in 17 ketosteroid excretion in cirrhosis[5] Testosterone, which has a hydroxyl group on carbon atom 17, is much less active in stimulating the prostate than the androgens, such as androsterone, with a ketone group at C17[6] If the fall in ketosteroid excretion in cirrhosis is due to inadequate oxidation of the testosterone type of androgen to the androsterone type, then the stimulus to prostatic hypertrophy would be much reduced It is apparent, however, that until more is known of the ætiology of benign prostatic enlargement, any explanation of the inhibitory effect of cirrhosis can only be speculative Nevertheless, this effect of cirrhosis strongly supports the hormonal-imbalance theory, and encourages the view that prophylaxis, and perhaps treatment, may one day be successfully achieved by hormone therapy alone

CLOSURE OF THE LARYNX

THE comparative anatomical studies of Negus[7] indicate that the larynx is primarily a sphincteric mechanism designed to prevent the entry of water or other noxious substance into the lungs and to regulate the flow of air to and from the lungs, the production of sounds appears to be a later development Complete or partial obliteration of the laryngeal lumen during vocalisation, swallowing, and other manœuvres is usually described as closure of the glottis (apposition of the vocal cords) It is believed that the vestibular folds may prevent expiration, but they are not thought to play any part in normal phonation Muscular closure of the superior aperture of the larynx was described by Stuart[8] By means of cineradiography in the anteroposterior and lateral projections, combined with the usual method of examination, Ardran et al[9] have obtained further information on laryngeal behaviour

During quiet breathing the laryngeal lumen is wide open and little movement takes place The vocal folds are turned upwards over the laryngeal ventricles so that the airway is not obstructed When closure occurs the whole of the airway from the level of the vocal folds to the superior aperture of the vestibule is obliterated by sphincteric muscular action Complete or partial closure may take place while holding the breath, coughing, performing any act that requires rigidity of the trunk muscles, and swallowing There is also a mechanism whereby the vocal folds are turned down across the airway with narrowing of the airway above, and speech is always associated with partial closure of the vestibule and vestibular folds

This sphincteric closure of the larynx from the level of the vocal folds upwards protects the airways during the act of swallowing[10], the epiglottis turns down over the mouth of the larynx, but this happens only towards the end of the act of swallowing and after the bulk of the bolus has passed the entrance to the larynx, which may still be open at the time A little of the bolus commonly enters the vestibule and may even descend as far as the ventricle without causing coughing and without the subject being aware of the fact In normal people this portion of the bolus is always expelled on the obliteration of the laryngeal lumen when the last of the bolus leaves the pharynx Patients with a disorder of the larynx—for example, in acrosclerosis[11]—may fail to clear the vestibule of bolus residues in the normal way

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[1] See *Lancet* 1952 i 300
[2] *Ibid*, 1952 ii 477
[3] H. H, Wilens, S L *Arch. intern. Med* 1953 91, 304
R I *In* The Hormones. New York 1950 vol. 2,
[5] Schedl, H P Ditto K., Bean, W B *J Lab clin Med* 1953, 42 116
[6] Selye H Textbook of Endocrinology Montreal, 1947, p 613.
[7] Negus V E Comparative Anatomy and Physiology of the Larynx. London 1949
[8] Stuart, T P A *Proc roy Soc* 1891–92, 50 323
[9] Ardran G M, Kemp F H Manen L *Brit J Radiol* 1953 26 497
[10] Ardran, G M Kemp, F H *Ibid* 1952 25 406
[11] Ardran G M Kemp F H, Truelove, S C *Gastroenterologia, Basel*, 1953 79 361

Special Articles

MARRIAGE AND CHILDBEARING IN ELATION TO CANCER OF THE BREAST AND UTERUS

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CANCER of the breast has long been recognised as ommoner in single than in married women, and the fference has usually been attributed to the protective fects of pregnancy or lactation. Cancer of the uterus n the other hand, is commoner in married than in single omen, and one of the reasons usually given for this that childbearing increases liability to cancer of the erine cervix. Thus Gagnon (1950) found no case of ncer of the cervix in a twenty year survey of 13 000 anadian nuns. These different tendencies for mortality om cancer of breast and uterus in relation to marital atus for England and Wales in 1948–49 are shown in ble I As the age distributions of married and of ingle women are very different, the crude rate for all emales aged 15 or more would give a misleading omparison, and standardisation has been carried out y means of the equivalent average death rate—i.e., he simple average of the rates at each of the seven ge-groups shown

ABLE I—MEAN ANNUAL DEATH RATES FROM CANCER OF BREAST AND OF UTERUS PER MILLION WOMEN SINGLE AND MARRIED, BY AGE, IN ENGLAND AND WALES 1948–49

Age (yr)	Breast		Uterus	
	Single	Married	Single	Married
-24	1	1	1	4
-34	21	33	13	23
-44	230	200	68	83
-54	663	469	174	294
-64	935	738	333	318
-74	1319	1003	451	604
or more	2044	1423	567	625
quivalent average death rate for females aged 15 or more	746	552	230	308

That the relation between marital status and cancer f the uterus involves mainly cancer of the cervix is ndicated by table II, which compares mortality certified s due to cancer of cervix, body of uterus, or simply of terus without *further details of site. At older ages* he last group unfortunately greatly outnumbers the wo others. Mortality from cancer of the cervix was about wice as high in married women as in single women Cancer of the body showed little difference between the wo classes of women but what difference there was ndicated a small excess among single women The ndefined group of uterine cancers, presumably composed ainly of cancers of cervix and of body in their natural roportions, showed some excess in the married group s would be expected because of the effect of the cervix ases it contained. The equivalent average rates at ges 15 and over in tables I and II can be summarised as ollows

	Single	*Married*
Breast	746	552
Uterus	230	308
Cervix	*62*	*137*
Body	*39*	*31*
Uterus other	*128*	*139*

Since 1921 Australian mortality statistics have distinguished between cancer of various sites among single women, married childless women and married women who have borne children Dorn (1943) analysed these Australian data for various sites including breast and genital organs. For the years 1919–23 the standardised death rates per 100,000 were as follows:

	Never married	*Married without children*	*Married with children*
Breast	40	34	24
Female genital organs	*30*	*44*	*33*

From these figures it was concluded that motherhood protected against cancer of the breast, but it was also suggested that mortality among married women without children was less than among single women partly because a higher proportion of married childless women than single women probably become pregnant and in addition the mortality of married women is in general lower than that of single women

Cancer of the uterus was not shown separately for 1919–23 in the Australian data, but Dorn was able to *distinguish it separately for 1931–35* obtaining the following relatives indices, married women with children being taken as 100

	Married with children	*Single*	*Married but childless*
Breast	100	145	137
Uterus	*100*	*80*	*137*

As the Australian census of 1933 did not enumerate the two classes of married women separately, the above indices were calculated upon populations assumed to be in the same proportions as deaths from all causes an assumption which though not strictly correct would not seriously invalidate the conclusions drawn—namely that motherhood protects against cancer of the breast and that childless married women had the highest mortality from cancer of the uterus, and single women the lowest

Johnstone and Hosker (1948) also studied the Australian statistics and were led to two possible conclusions

> " (*a*) that circumstances attendant on marriage as such, in contradistinction to procreation exert some influence on cancer of the breast and of the uterus
>
> (*b*) that some obscure form of selection favours nuptiality among people less prone to malignant disease at one site or more prone to malignant disease at another

In England and Wales since 1938 information has been obtained at death registration as to whether or not *a woman who had been married had ever had children.* Those who had had children have been designated 'fertile,' and those who had not had children " infertile These terms apply not to the ability of the woman to have children but simply to whether or not she had in fact had any Analysis of the proportions of women dying infertile among women dying from various causes, including cancer of breast and of uterus have been published by the Registrar General (1947 1951) and discussed in the Statistical Reviews for 1938–39 and 1940–45 , and a much fuller analysis, based upon pro-

TABLE II—*MEAN ANNUAL DEATH RATES FROM CANCER OF* CERVIX AND BODY OF UTERUS PER MILLION WOMEN SINGLE AND MARRIED BY AGE, IN ENGLAND AND WALES, 1948–49

Age (yr)	Cervix		Body		Uterus not further defined	
	Single	Married	Single	Married	Single	Married
15–24	—	1	—	—	1	3
25–34	7	15	1	0 4	4	7
35–44	32	63	7	4	23	28
45–54	61	170	28	18	84	107
55–64	90	239	63	62	174	208
65–74	116	254	83	68	52	281
75 or more	128	207	87	78	352	341
Equivalent average death rate for females aged 15 or more	62	137	39	31	128	139

portionate mortality from all causes is given in the text volume for 1948–49 (Registrar General 1953), where mention is made of the "complex interplay of selective influences" that complicate the interpretation of the rates for the different marital and fertility classes, particularly at the marrying and childbearing ages

Although annual estimates of the numbers of single and married women of different ages in the population are *regularly available, the proportions of living married* women who have or have not had children is not usually known However, the 1% sample results of the 1951 Census (Registrar General 1952) give the proportions of fertile and infertile married women up to age 50 These proportions, together with the proportions of deaths from all causes at ages over 50 among fertile and infertile married women, have been used to calculate death rates at separate ages in relation to the populations at risk in 1948–49 for the various marital and fertility classes

That populations at risk estimated from numbers of deaths from all causes are not satisfactory at younger ages but are probably adequate at ages 45 and over can be concluded from the following figures showing the proportions of (*a*) childless married women among all married women at the 1951 census , and (*b*) deaths from all causes in 1948–49 of childless married women among deaths from all married women

TABLE III—MEAN ANNUAL DEATH RATES FROM CANCER OF BREAST PER MILLION WOMEN, SINGLE, MARRIED INFERTILE, MARRIED FERTILE, AND WIDOWED AND DIVORCED, BY AGE, IN ENGLAND AND WALES, 1948–49

Age (yr)	Single	Married infertile	Married fertile	Widowed and divorced
15–24	1	—	3	—
25–34	21	25	35	65
35–44	236	260	189	278
45–54	663	512	458	512
55–64	935	900	705	806
65–74	1310	1267	956	1111
75 or more	2044	1918	1337	1764
Equivalent average death-rate for females aged 15 or more	746	697	526	648

Age	(*a*)	(*b*)
15–	0 480	0 469
25–	0 210	0 274
35–	0 157	0 209
45–	0 206*	0 200
55–	—	0 168
65–	—	0 150
75 +	—	0 149

* Ages 45–49 only

By ages 45–54 the difference between the two proportions is negligible, and probably remains so at higher ages

Cancer of Breast

Death-rates per million women by age and by marital and fertility status are shown in table III The equivalent average rates for single and for childless married women (746 and 697 per million) were higher than the average rate for fertile married women 526 per million—i e , cancer of the breast was lower among women who had borne children Intermediate between these two sets of rates came those for widowed and divorced women 648 per million At ages under 35 the rates for fertile married women were higher than those for infertile married women This apparent reversal of the cancer risk among young women compared with old is almost certainly not fortuitous but indicates that at these ages fertile women are more liable than infertile women to die from cancer of the breast, although the opposite occurs at later ages The same sort of relationship was noted by Dorn (1943) in the Australian data for 1919–23 and [illegible] as of no importance, because of the [illegible]ers of deaths involved , but it was subsequently noted again in the English data for 1938–39 (Registrar General 1947) and 1940–45 (Registrar General 1951) Proportionate death rates for 1948–49 (table IV) confirm that there is a difference in the behaviour of cancer of the breast in relation to fertility at child bearing ages compared with older ages But, though the rates in table III suggest that the class of younger women particularly liable to die from breast cancer is the fertile married group aged 25–34, the proportionate rates (table IV), while confirming this tendency, also suggest that in the next age-group (35–44) both classes *of married women, fertile and infertile, are more liable than unmarried women to die from cancer of the breast.* Whereas there is clear evidence that after the child bearing age women who have borne children are less liable than women who have not, whether married or unmarried, to die from cancer of the breast, this relationship does not hold during the childbearing years, where childbearing or possibly the marital state itself seems to *predispose to death from cancer of the breast* The equivalent average rates for all ages over 15 are influenced mostly by the high rates of older ages, and show that the average risk is less among fertile than infertile married women , but they conceal the important departure from this relationship at younger ages

TABLE IV—PROPORTIONATE DEATH RATES FROM CANCER OF BREAST PER 10 000 DEATHS FROM ALL CAUSES, SINGLE, MARRIED INFERTILE, AND MARRIED FERTILE WOMEN, BY AGE, IN ENGLAND AND WALES, 1948–49

Age (yr)	Single	Married infertile	Married fertile
15–24	7	—	94
25–34	91	134	271
35–44	684	925	956
45–54	1071	1073	940
55–64	749	776	613
65–74	423	413	314
75 or more	199	261	185
Proportionate equivalent death rate for females aged 15 or more	461	512	472

TABLE V—MEAN ANNUAL DEATH RATES FROM CANCER OF UTERINE CERVIX PER MILLION WOMEN, SINGLE, MARRIED INFERTILE, MARRIED FERTILE, WIDOWED AND DIVORCED, BY AGE, IN ENGLAND AND WALES, 1948–49

Age (yr)	Single	Married infertile	Married fertile	Widowed and divorced
15–24	—	—	1	187
25–34	7	8	17	20
35–44	32	48	54	108
45–54	64	139	178	274
55–64	90	187	273	319
65–74	116	212	262	286
75 or more	128	180	211	301
Equivalent average death-rate for females aged 15 or more	62	111	142	211

Cancer of Uterine Cervix

The equivalent average death-rates for infertile and fertile married women were about twice that for unmarried women, the rates being respectively 111, 142, and 62 per million (table V) For widowed and divorced women the rate was 211 In contradistinction to the rates for cancer of the breast, there was no variation in the marital and fertility relationships at different ages , and, although at each age parous women fared worse than those who had not had children, the factor of marital status apart from fertility also conduced to cancer of the cervix

Cancer of Uterine Body

The equivalent average death rates in table VI indicate that single and nulliparous married women both had a ater tendency to die from cancer of the uterine body an had parous married women, the rates being pectively 39, 41 and 29 per million Widowed and orced women gave intermediate rates averaging 36 r million. Although the average rates for all ages er 15 suggest that the fertile married women enjoyed me advantage the rates at individual ages do not show is tendency with complete consistency At ages 75 d over the fertile married class gave higher rates than l infertile married women ; this exception is possibly no significance

Cancer of Uterus not Further Defined

Table VII gives the rates for those deaths from cancer the uterus that could not be assigned to either of the o more specific sites. The equivalent average rates re highest for widowed and divorced women and for ertile married women The figures are provided to mplete the picture, but, since they mainly represent ill-defined mixture of cancer of two sites where the haviour of the disease has been shown to be quite fferent in relation to marriage and fertility, it would rve no useful purpose to discuss them in detail.

LE VI—MEAN ANNUAL DEATH RATES FROM CANCER OF BODY OF UTERUS PER MILLION WOMEN, SINGLE MARRIED INFERTILE, MARRIED FERTILE, WIDOWED AND DIVORCED BY AGE, IN ENGLAND AND WALES, 1948–49

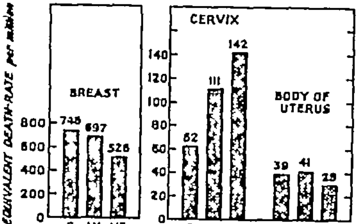
Age (yr)	Single	Married infertile	Married fertile	Widowed and divorced
-24	—	—	—	—
-34	1	—	1	—
-44	7	6	3	3
-54	28	27	15	23
-64	63	61	49	56
-74	83	103	68	80
or more	87	96	80	80
uivalent average death rate for females aged 15 or more	39	41	29	36

Discussion

Though the statistics given in the various tables ad in the figure indicate clearly that there are definite lations between marital and fertility status and ancer of the breast and uterus they do not necessarily nply direct causal relationship—i e. that marital or rtility status per se predisposes to or protects gainst, cancer at these sites. Several factors have o be taken into consideration before conclusions can e drawn One is the more favourable mortality xperience in general that is nowadays enjoyed by narried women compared with single widowed and livorced women Thus the equivalent average rates rom all causes in 1948–49 per 1000 women aged 15 r more were married women 18, single women 23 and ridowed and divorced women 27 A second factor is hysical selection for marriage and for childbearing, women suffering from chronic ill health are on the whole less likely to marry or if married are less likely to have children than other women This applies mainly to women dying within the age groups at which marriage and child bearing mainly occur though in the case of diseases of very long duration the influence of selection of this kind may continue to later ages. So far as cancer of the breast and uterus are concerned, the influence of physical selection may be of some importance, though not much, at ages under 45 and of even less importance at older ages A third consideration assuming that an apparent relationship is in fact a causal one is the direction in which this causal influence is operating For example, is it the marital status that conduces towards death from cancer of the cervix, or does a tendency towards ultimate death from cancer of the cervix due for instance to some hormonal diathesis, render a woman more likely to marry ?

TABLE VII—MEAN ANNUAL DEATH RATES FROM CANCER OF THE UTERUS NOT FURTHER DEFINED PER MILLION WOMEN SINGLE, MARRIED INFERTILE, MARRIED FERTILE, WIDOWED AND DIVORCED, BY AGE, IN ENGLAND AND WALES, 1948–49

Age (yr)	Single	Married infertile	Married fertile	Widowed and divorced
-24	1	3	3	—
-34	4	7	7	13
-44	28	37	26	36
-54	84	103	107	159
-64	174	239	201	237
-74	252	331	273	334
or more	352	395	310	400
Equivalent average death rate for females aged 15 or more	128	145	138	10[illegible]



Equivalent average death-rates per million from cancer of breast, uterine cervix and body of uterus in females aged 15 or more in England and Wales in 1948–49 : S, single ; MI married infertile ; MF married fertile.

Though the factors just mentioned ought not to be ignored, their importance should not be exaggerated they are not likely to explain the very wide differences in the tabulated mortality rates for the different marital and fertility groups, and it is a reasonable conclusion that a woman's marital and childbearing experience does to an important degree determine her risk of dying from cancer of the breast and of the uterine cervix A question that remains to be settled is whether the mortality experience of fertile women depends on the number of children they have borne as distinct from simply having borne at least one. No help on this point comes from either Australian or English vital statistics, but the report by Smithers et al. (1952) on cancer of the breast gives some data concerning the actual number of fertile women aged 45 or more found to have cancer of the breast, classified according to the number of children they have had compared with the calculated expected number of women with breast cancer in each parity group The results are summarised in table VIII which suggests that it is not just the fact of having borne a child but the number of children borne that gives fertile women over 45 their reduced risk of cancer of the breast.

TABLE VIII—ACTUAL AND EXPECTED NUMBERS OF WOMEN WITH BREAST CANCER ACCORDING TO NUMBER OF CHILDREN (AFTER SMITHERS ET AL. 1952)

No of children	No of women aged 45 or more with breast cancer	Expected no of women	Ratio of actual no. to expected no.
1–3	184	154	1 19
4–6	48	65	0 74
7 or more	21	34	0 62

Summary

Death rates from cancer of the breast in women who have passed the childbearing age are higher in single and in infertile (i e, childless married women) than in fertile married women (i e, married women who have borne children) At childbearing ages, however, married women, whether they have had children or not, have higher death rates from cancer of the breast than do single women

Death-rates from cancer of the uterine cervix are higher in married than in single women at each age Marital status alone, apart from childbearing, seems to be a factor causing this higher mortality

Death rates from cancer of the body of the uterus tend to be higher in single and in infertile married women than in married women who have had children

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GENERAL MEDICAL COUNCIL

SESSION, NOV 24–27

Sir David Campbell's presidential address to the council was reported last week

Dr H GUY DAIN, presenting the report of the Pharmacopœia Committee, said that sales of the *British Pharmacopœia, 1953*, totalled 25,358 The British Pharmacopœia Commission, 1953–58, held its first meeting in October

The council found the arrangements for compulsory internship by the University of Hong Kong satisfactory for registration under the Medical Act, 1950

Medical Disciplinary Committee

The committee, with the president in the chair, at its first sitting, on Nov 25, heard three applications for restoration of names to the Register

The committee, after hearing evidence, directed the registrar to restore the name of *Stewart Quarterman Servanté.*

The committee did not think fit to direct the registrar to restore the names of *Arthur James Daly* and *Sumatapalage Reginald Gunewardene*

POSTPONED JUDGMENTS

At their sitting in November, 1952, the committee had postponed judgment on *James Watson Richmond* Dr Richmond appeared and presented testimonials. The registrar was not directed to erase his name from the Register

Judgment had also been postponed on *William Pitt,* who presented testimonials The registrar was not directed to erase his name

Judgment had been postponed last November for one year on *Gerald Francis Adye Curran* In view of the testimony which he produced the committee directed the registrar not to erase his name

The committee took the same course with *Archer Wilson Dunn,* against whom judgment had also been postponed for one year

ALLEGED FRAUD

Oscar Drexler, registered as of 18, Grosvenor Square, London, W 1, M D New York (1929), was charged with having wrongfully retained in his possession £65 entrusted to him by Mr Edward Valentine Nowak for payment to an obstetrician for professional services to Mrs. Nowak's confinement In January, 1953, Mr Nowak received an account from the obstetrician He took it to Dr Drexler, whose explanation was that the money was paid and that there had been an error In May Mr Nowak received a second account Dr Drexler said it had been paid A writ was issued It was not until after a complaint had been made to the General Medical Council that the £65 was given to the obstetrician Dr Drexler, giving evidence on his own behalf, said that he the time been in the midst of domestic trouble, and glected many things. The committee determined that the facts were insufficient, and they accordingly fo Dr Drexler not guilty of *infamous conduct in a* professio respect

John Joseph Flanigan, registered as of 25, Church Str Coatbridge, Lanarkshire, M B Glasg (1947), was charged w having been convicted in the Sheriff Court, Lanarksh of causing to be posted to the executive council for the coun maternity medical service claim forms in which he preten that an anæsthetic had been administered by another doc and thus obtained additional fees His sentence of 60 d imprisonment was varied on appeal to the High Court Justiciary to a fine of £25 with the alternative of three mont imprisonment Mr J Wheatley, for Dr Flanigan, said t this was a case of careless, negligent conduct rather than intention to perpetrate a fraud on the National He Service Dr Flanigan had paid the money back to executive council That his culpability was not g was a view shared by the Lord Justice General in his judgm in the appeal The president announced that the commi were unable to accept the statement that the circumsta in which Dr Flanigan committed the offence afforded justif tion for his actions They were, however, prepared to t into consideration the assurance given for his future cond and postponed judgment for one year

William Acton MacIlrath, registered as of Wyncroft, Kn Belfast, M B Belf (1928), appeared on a charge of infam conduct in a professional respect The charge alleged tha had disregarded his personal responsibilities to his Nati Health Service patients by accepting full time employmen Cane Hill Hospital, Coulsdon, Surrey, while carrying o general practice at 222, Lewisham Way, London, S.E 4, that he fraudulently claimed and received from the Lon Executive Council grants amounting to £697 towards salary of a trainee assistant and the supervision fee when reason of his employment in a whole time capacity (which wrongfully concealed from and/or failed to disclose to Council) he was unable to give to any trainee assistant suffic supervision and/or training The N H S committee wh inquired into the arrangements for the running of his prac fined him £1000 [1] The N H S Tribunal had recommen that his name should be removed from the list, and on ap the decision of the tribunal was upheld by the Minis

After consideration in camera the President stated that committee regarded with the gravest concern the facts wh were proved They were unable to regard the statements m by Dr MacIlrath as affording the slightest justification of actions, which they regarded as deplorable Neverthel after careful consideration of all the circumstances and of assurances which had been given concerning his fut conduct, they were prepared to give him an opportunity implementing those assurances They would therefore po pone judgment for two years, until the meeting in Novem 1955, but they would expect him to appear again before th at the end of one year

Gerald Niall Monaghan, registered as of The Beeches, Alb Road, Dublin, L R C.P.I (1945), was charged with having b convicted at Shrewsbury assizes of five offences of obtain credit and of engaging in trade while a bankrupt T President announced that the committee regarded a convict of this nature as disgraceful for a medical man, but to g Dr Monaghan an opportunity to reconsider his conduct a to rehabilitate himself, they had determined to postp judgment for one year

IMPORTUNING

Ratan Noshirwan Bulsara, registered as c/o Bank of Ind 17, Moorgate, London, E C 2, M.B Bombay (1945), had b convicted at West London Magistrates' Court for persisten importuning male persons The committee felt it their d in the public interest to satisfy themselves as far as possi that the incident in question was an isolated event and r indicative of a habit Judgment was postponed for one ye

DRUNKENNESS IN CHARGE OF A CAR

Patrick Kennedy, registered as of 53, East Dulwich Ro London, S E 22, L R.C.P I (1926), appeared for postpon judgment After considering the report given by his medi adviser, the Committee decided to postpone judgment for further period of six months udgment had been postponed against *Patrick Joseph* lin registered as of 1, North Terrace, Mardy Ferndale m., M.B. N U.I (1920) who had been convicted of being charge of a motor-car while under the influence of drink e President announced that the committee had learned h concern that during this period Dr Conlin had been victed of a further offence of a similar nature Judgment further postponed for one year

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[1] See *Lancet,* 1952, i, 260

Illiam Francis Hirsch Coulthard registered as of Balwin n, Aspatria Carlisle M.B Edin. (19-7) admitted a con tion for driving a motor vehicle when under the influence drink Dr Coulthard had appeared before the council in 6 on a similar charge The President said that the com ttee took a serious view of repeated offences of this kind they had determined to postpone judgment for one year

ugh Rinn, registered as of 324 Dudley Road Birmingham, M.B. Glasg (1923) admitted convictions in 1947 and in 3 of driving a motor-car while under the influence of drink drugs. Judgment was postponed for one year

ames William Hay, registered as of 51 Spencer Street, lisle, M.B. Aberd. (1924) had been convicted of driving a tor vehicle when under the influence of drink or drugs

Hay had been before the committee in May 1951 when gment was postponed his name had not been erased. President announced that in order to give Dr Hay one further opportunity of overcoming his tendency to drink to excess, the committee had determined to postpone judgment for one year

DANGEROUS DRUGS

Joseph Hirschmann, registered as of 118 Maida Vale London, W 9 M.B Dubl (1920), had been convicted at the court of summary jurisdiction Clun of offences of procuring pethidine Dr Hirschmann's authority to prescribe dangerous drugs had been withdrawn in 1936, and had never been restored. He had 1000 patients and was on the obstetric list for the county of Salop

Mr F P Neill counsel, said that pethidine was obtainable in 1939 but was not in common use It became popular during the war and was used in obstetrics. It had later been added to the list of dangerous drugs so that what had been a proper course of action became an unlawful practice for Dr Hirschmann. But he continued to use pethidine because he believed his prohibition covered only drugs to which the Act applied at the time of his prohibition. Under the latest regulations any midwife was allowed to prescribe this drug Dr Hirschmann had made arrangements with a deputy to prescribe other dangerous drugs. He obtained pethidine openly There was no suggestion that the drugs had been put to any improper use The committee postponed judgment for one year

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Personal Papers

CHRONIC OSTEOMYELITIS

THE purpose of this account is to show how chronic deed is this disease. The duration of my own case for enty-six years is interesting, because the start was in e days when acute osteomyelitis was not uncommon children, particularly of poor economic status, and the ortality was high. Today it is uncommon, the mortality very low and chronic osteomyelitis is becoming a rity the last two facts being due to the advent of tibiotics This account will also show that I am obably right in not writing of the finish" of my case ing in such and such an era, it is, I suggest a rash ctor who pronounces a case of *chronic* osteomyelitis red.

* * *

Twenty-six years ago then, at the age of eight years, though my economic status was not unhappy and I as bronzed at the end of a South Coast holiday a dical attack of acute osteomyelitis started out of the ue in the right upper tibia. The general practitioner -forever afterwards hero and friend—was on to the agnosis like a knife. I use the metaphor purposely ecause the surgeon was not After some three weeks which the knife was used to relieve pockets of sub taneous pus and cellulitis and a severe septicæmia as fought apparently with sublime innocence and the lp of a Divinity I was moved across ngland to a teaching hospital (The emory of that journey is as clear today s it was hazy and surrealistic at the time) here my rapidly ebbing young life was aved by widely stripping and guttering he right tibia, and draining a metastatic bscess which had formed in the left rsus.

From this time, with a gradually developing bony (mercifully not fibrous) ankylosis of the right knee-joint and left ankle-joint I became a case of chronic osteomyelitis.

Two years later the sinus over the right tibia stopped discharging after many sequestrectomies, and the left ankle sinuses, after a similar history healed four years later I can recall now the day of the week on which the memorable night arrived when I went to bed without a bandage on either leg The cool sheets even now can be felt touching my ankle

The behaviour up to the present time is shown in the accompanying figure. The state of the sites is divided into five categories:

(1) *Quiescent*—This means absence of pain and the ability to lead a busy schoolboy undergraduate medical student or doctor life unhindered

(2) *Recurrence Threatened but no Incapacity*—Signifying pain and the subjective knowledge born of experience that a flare up was imminent but the current mode of life was little interfered with

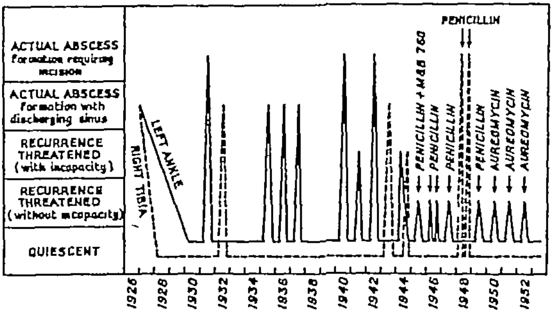
(3) *Recurrence Threatened with Incapacity*—Tenderness and muscle spasm made walking impossible

(4) *Abscess Formation with Discharging Sinus*—Usually by way of the spontaneous breakdown of an old scar or sinus.

(5) *Abscess Formation requiring Surgical Aid*—The collection of pus was localised and large

* * *

None of the recurrences lasted more than three months; the average was six weeks. There was no significant seasonal factor My general health has been excellent throughout except for an attack of acute appendicitis in 1947 I have tried to determine any cause for the recurrences. The figure shows that the only years free from these were 1933 and 1934, and 1938 and 1939 During the former I was as active as I shall ever be, no doubt, at boarding-school while during the latter I was an undergraduate and the period included a working trip to the Arctic Circle. I mention this because using



Course of illness, showing treatment of recurrences.

the affected limbs or parts somewhat rigorously is not therefore a cause, as is often claimed in teaching What is interesting is that the total recurrences of all kinds in the ten years preceding the beginning of the late war were 5 The total in the next ten years was 13, although 4 were "threatened but non-incapacitating" Perhaps the rather strenuous mental and physical working conditions during and after the war years had something to do with it

The other striking feature shown by the figure is that since 1945 there have been 10 recurrences The responsible organism is *Staphylococcus aureus*; and penicillin, and latterly aureomycin, have been used in big dosages with each warning of a flare-up In the case of the left ankle it will be seen that no recurrence has reached the "incapacity" level The right tibia, however, on 2 occasions (and the only 2 in the same year) broke loose and reached the operation stage (We even tried—my long suffering and patient colleagues and I—intra-arterial penicillin on the first of these occasions, via the right femoral artery The idea was to produce a sudden great concentration of penicillin in the by-now hyperæmic guilty cavity area Perhaps it did, but it did not stop the march of events For those interested, it *did* produce a great amount of temporary pain and the sensation that the lower limb was alternatively going to blow up or possibly melt with fire I hasten to add that my friend the surgeon who gave the intra arterial injection did so against his normally perfect judgment, but I was so difficult and unpleasant to him that I upset this quality I only hope he has by now forgiven me for the subsequent nightmares I later learned that he had suffered—the general theme running on the lines of arterial spasm→ gangrene→amputation)

* * *

In 1949 I became sensitised to penicillin and suffered an attack of giant urticaria, œdema, and pyrexia all rolled into one From then onwards aureomycin has been used By inspection of the diagram, it does seem possible, then, to keep the recurrences down on the lower level, at least in the case of the left ankle, but not to lessen the recurrence *rate*

Other points worth mentioning are that, as shown in the case of the right tibia, a quiescent period of eleven years can lull you into a false sense of security, that, in the great majority of the attacks, general constitutional upset lasted only a few days at the beginning of a recurrence, and that pyrexia has always been strikingly absent, as has sequestrum formation after the original healing One recurrence was ushered in with great ceremony by a rigor, but this sole occurrence led to a very minor affair

* * *

The most pertinent question is, How can you stop recurrences altogether? All authorities agree that the great obstacle to treatment is the fact that cavities and infected bone are very difficult to reach with antibiotics carried in the blood stream, for extensive thrombosis of the nutrient vessels and stripping of the periosteum occur in the early attack (Altemeier and Wadsworth 1948) Many methods of treatment have been tried those of Winnett Orr (1927), Baer (1931), Albee (1933), Kornev (1937), and Buchman (1937) are examples of the many diverse techniques from maggot therapy to staphylococcus toxoid The sulphonamides have not been very successful in the treatment of chronic osteomyelitis The only radical cure seems to be to remove all infected bone and to saucerise all cavities, at the same time bringing antibiotics into direct contact with the areas This is advocated and described by Basu (1951), using aureomycin as the antibiotic, but his follow-up period in 30 cases with no recurrence was never longer t[illegible] six months, and a glance at the figure will show why [illegible]st wait a considerable time before judging the efficacy of this method The surgical difficulty of removin all possibly infected bone is great, especially in long standing cases of extensive bone involvement

The possible mechanism of preventing recurrence becoming incapacitating is that, when a flare-u threatens, the area becomes inflamed and there is great increased vascularity This aids the carrying of a antibiotic to the required area In most recurrences i will at least apparently prevent an escape or extensio of the infection It does seem, however, that, even i shamefaced, the organism returns to lurk behind a avascular wall It is hard to have to wait for a reappear ance before dealing with it, but there it is. At present then, it looks as though aureomycin, which has bee shown to be particularly effective against coagulase positive *Staph aureus* (Nichols and Needham 1949), use systemically has a place in the treatment of chron osteomyelitis

* * *

For obvious reasons this essay must be anonymou I want to take this opportunity of expressing my dee gratitude for constant skill, patience, and kindness fro so many doctors and friends, and to my parents an wife But, alas, they must all be anonymous too

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Medicine and the Law

A Transfusion Accident

In an action [1] before Mr Justice Hilbery and a jur in the Queen's Bench Division, the plaintiffs sought t prove negligence in the administration of a bloo transfusion to a 26 year old man on the day of his deat The man's parents claimed damages from the Southen group hospital management committee, and the counsel brought evidence to show that the blood use in the transfusion was infected and that death wa caused by "toxæmia due to infected blood" and not b incompatibility

The patient was admitted to Southend General Hospita on Oct 28, 1951, and an operation for hæmorrhoids wa performed The operation was successful and it was no until a week or so later that repeated bleeding made i necessary to give him transfusions. The fourth trans fusion on Nov 18 produced rigors, nausea, and pyrexi and had to be abandoned The patient recovered fro this reaction, but he was still very anæmic, and the senio surgical registrar thought it was advisable to give hi more blood in case he had another hæmorrhage afte leaving hospital On Nov 21 the fifth transfusion wa given rigors, nausea, vomiting, and pyrexia followed By 5 P M that day the patient's temperature was ove 103 and his pulse was imperceptible Despite a treatment, he died at 8 P M

A pathologist from another hospital, who had carri out a post mortem examination on Nov 26 at th request of the coroner, said that his conclusion was tha death had been due to the presence in the blood-stream o bacilli "foreign to the body but commonly found i water and soil" The organism isolated was a moti gram-negative rod which grew well at 20°C but hardly a all at 37°C—probably an atypical coliform There wa no question, he added, of the blood-groups being incom patible In the circumstances, he thought that every thin pointed to the fact that the blood given in the transfusio ov 21 contained an enormous number of organisms reply to a question from defendant's counsel he ed that fatal reactions could be caused by the ence in the transfused blood of dead bacilli which ld be extremely difficult to detect. This could happen out negligence on anybody s part

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[1] *Times* and *Manchester Guardian*, Nov 26, 27 and 28, 195

he pathologist at Southend General Hospital said from the tests he had performed he had concluded the patient's reaction to the non fatal transfusion of 18 was due neither to incompatibility nor to ction. He was not surprised that evidence of infection been found in an examination carried out five days r death. He thought it likely that the blood stream been infected from the operation site On the data lable, he was unable to say that the patient had from toxæmia due to the transfusion of the infected od, something in the blood had been responsible but he moment he could not say what. It was stated the blood used for the fatal transfusion was later cked and rechecked for sterility and compatibility was found to be correct Unfortunately during the for the patient s life the bottle was left uncapped he ward, and it was later found to be infected.

he patient s family doctor also gave evidence He ted the young man on Nov 20 when he seemed much ter and was expecting to leave hospital shortly He reluctant to have another transfusion but he was suaded to do so In his doctor's view, the transfusion Nov 21 after the reaction on Nov 18 was an error of gment. He agreed that two hæmorrhages after such operation was a serious matter, but he did not think t a hæmoglobin of 40–44% was dangerously low

t was stated for the plaintiffs that the action was inally brought also against the house-surgeon who given the transfusion This doctor could not now be ced, and counsel for the plaintiffs sought to show that was not registered with the General Medical Council the time in question, though, as Mr Justice Hilbery erved, this was irrelevant to the issue of negligence, the house-surgeon was fully qualified and the M.C. would have granted registration had he applied it.

iving judgment for the defendants, Mr Justice bery said there was no evidence on which a jury could sonably find for the plaintiffs The allegation that the spital was negligent in entrusting the transfusion to a ng man recently qualified was absurd particularly ce the evidence was that, in the opinion of highly alified surgeons under whom he worked, this young ctor was exceptionally competent. The allegations in s case indicated recklessness in making charges of gligence. There was nothing to show that the bottle question had become infected because of the way in ich it had been handled by the house-surgeon or anyone e.

Public Health

Eire in the Second Quarter

In Eire during the June quarter of this year[1] the birth-te was 22 8 per 1000 population this was 1 0 below e rate for the second quarter of 1952 The death te was 12 1 per 1000 population (0 3 above that for the cond quarter of 1952) The death rate from tuber-losis was 0·5 per 1000 population (respiratory 0·4 ther forms 0 1), compared with 0 6 (0 5 and 0 1) in the cond quarter of 1952 The maternal mortality rate s 0·7 per 1000 births registered compared with 3 for the second quarter last year; and the infant-rtality rate was 41 per 1000 compared with 35 for e second quarter last year

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[1] Quarterly Return of the Marriages, Births and Deaths registered during the June Quarter 1953. Obtainable from the Government Publications Sale Office, G P O Arcade, Dublin. Pp 31 6d.

In England Now

A Running Commentary by Peripatetic Correspondents

THE electric telegraph the telephone, and wireless rank high among the great inventions of the past century But, as I have learned, our precipitate progress has not stopped there. Let me first trace in the background

My wife and the milkman have never been on terms of close accord For some years after the war he purveyed as well as milk, such rare delicacies as butter and eggs; and unruffled by the Minister of Food's dispositions he offered these to all who would buy Perhaps he was nettled by my wife s refusal to enter this *marché libre* but they got on well enough until she found that the wealthier customers could also obtain limitless milk and that our weekly portion was falling 2 pints short of what the Ministry deemed fair The ensuing scene ended all hopes of rapport. Each summer our milkman journeyed to Switzerland while we took ourselves to the Isle of Wight; but as time went on his market crumbled and last year we met him on the plage at Ventnor, and to our earlier differences is now added his bitterness at being *dragged down to our level* Accordingly my wife a tireless gadgeteer, began to cast around for an impersonal means of communicating her wishes to him, and she lighted on the answer This is a small half moon disc with a pointer that can be directed at anything from '10 gallons' at one end to ' none ' and " please knock at the other For a few days this device worked splendidly Then, one morning, we found 12 pints on the doorstep Taxed with this the next day, the milkman pointed mutely to the arrow and sure enough he had obeyed its instruction For three more days all went well but then he passed us by without allotting us so much as half a pint, and again we found that he had obeyed the machine A few mornings later the bell rang and on the doorstep my wife found the milkman. Each eyed the other watchfully Well?" said the milkman Well? said my wife The arrow was at please knock' This led us to examine our first premises. Did the fault lie with the machine or with a human element of which we had not taken account? Careful thought led us to conclude that the machine was not to blame There remained that vital human element Action followed swiftly I told our three little cherubs that the wind which next blew the arrow out of place would blow away their next Saturday's sixpences Now the machine is working perfectly

* * *

Those who view the elaborate armamentarium of the modern neurosurgeon with alarm and who secretly wish for the renaissance of a less complex surgical technique will be encouraged by a report[1] of an operation lately performed in Peru Two Peruvian surgeons had been interested for some time in Inca skulls, particularly those with trepanning holes; it seems that the Inca surgeons of 2000 years ago used stone chisels or knives made of obsidian for these operations. Using the ancient tools, the present-day surgeons have successfully removed a blood-clot from a patient s left parietal region They add that they were readily able to control bleeding from the scalp by the use of an ' Inca tourniquet —a one-inch wide bandage wound tightly thrice round the head Postoperatively the patient was given antibiotics—a sensible gesture although one calculated to annoy purists of primitive surgery

* * *

The help given to the National Health Service by doctor's wives is in my opinion not sufficiently recognised. True there is some appreciation of their book keeping and other auxiliary services for income-tax purposes. But I refer to their far more important *medical* work. I know of several like myself who, though without formal medical training, are much sought after for diagnosis, prognosis, and treatment or just for really authoritative advice. The reasons are obvious. In the first place we do not have to keep patients from asking awkward questions: such knowledge as we have, we share freely

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[1] *New York Times* Oct. 4 1953.

We do not need to examine our patients, nor do we even have to see them we can be conveniently consulted on the telephone or by post Unlike our husbands, we are unhampered by professional etiquette (Only last week did I have to tell a friend what I thought of Dr X for prescribing penicillin in a mild sore throat and to caution her against administering it to her little boy) Finally, we welcome inquiries on any medical subject and remain unaffected by the growth of specialism For instance, I feel I can be of help in such varied matters as boils, insomnia, bedwetting, ulcers, and slipped discs, though I must admit to a predilection for more obscure medical diagnoses involving less well-defined symptoms that baffle orthodox practitioners. Unfortunately in recent years, my friends, shopkeepers, and dailies present me increasingly with psychiatric and psychosomatic problems in which rapid success cannot be hoped for

But perhaps our greatest responsibility is in prescribing for our husbands "Are two aspirins enough, dear ?" mine asks me anxiously before embarking on a course of self-medication Where, indeed, would the Health Service be without us ?

* * *

A colleague of ours in the States whose interests run to comparative physiology told us of a harassing experience It appears that our colleague became interested in the matter of beavers, but was unfortunate enough to live in a virtually beaverless part of the country Accordingly, he issued an appeal to those of his friends who were more happily situated, and eventually his entreaties were answered by the totally unheralded arrival of a fine pair of beavers, escorted by a sceptical Railway Express man

The beavers had arrived, as beavers will, after all the technicians had gone home , and our colleague was at once placed in some difficulty, for the animal house was shut and he had no key However, he is a man of some resource, and he remembered a disused bathtub up in the attic He had no first-hand knowledge of the care and maintenance of beavers in bathtubs, but he had a vague idea that they would be happier with some water in the bath, so he dragged it over to a place where he could fill it from a convenient tap, and brought the beavers up to admire their new home Unfortunately the bath had in the course of time become detached from its plug, and our colleague cast about for a substitute Eventually he had a Machiavellian idea, and retrieved a large carrot from a bag of food outside the animal house With this he plugged the bath, partly filled it with water and tipped the beavers in, having provided them with some food This done, he went home, tired but happy, having locked the door on his charges

We need scarcely proceed further They *did* eat it , there *was* a flood In fact, the only unexpected feature of the proceedings was that the professor's desk was so nearly vertically under the bath The resulting interview was full of physiological suggestions, and at its close our friend found that rats would suit his purpose equally well

* * *

An important technique of the Bed-end Manner is the printing of the patient's name on his temperature chart in large block letters, legible at least two bed-ends away One can then say "How are you, Mr Blank ? and get undeserved credit for knowing every patient by name, as long as they stay in bed During the war when I had temporary charge of 1700 patients (in a 1400-bed hospital) I found it invaluable I could leave scientific impartiality to my junior officers with a good conscience In my old-fashioned way I sometimes thought my personal interest did more for some patients than the brilliant technology of my more gifted colleagues

* * *

Don t ask me to sit on your Brains Trust, Miss Denton.
Get someone more sprightly and glib
I ll sit, if I must upon boards till I bust
Or committees *ad hoc* or *ad lib*
But my cerebrovascular fittings
Are cobwebbed and riddled with rust
So if you are bent on this Brains Trust, Miss Denton,
 hold of some brains you can trust

Letters to the Editor

OPERATING-THEATRE INFECTION

SIR,—Your leader last week puts the responsibility eliminating operating-theatre infections squarely on t shoulders of surgeons I am not at all sure that surge alone can solve this problem

Dr Sevitt has reported in two articles—one in 194 and the other last week—3 major operating ro infections (1 of them fatal) occurring in a suite operating theatres in which over 10,000 operations h been performed during this period His investigati were asked for by the surgical staff of the hospi concerned, and his evidence accepted

In the same hospital there exists a dressing station the large wounds of burns and scalds, fitted with positive pressure ventilating system of clean air (enter at ceiling level and finding its exit at floor level) controlled trial of this system has confirmed that it only greatly reduces the number of organisms pres in the air but prevents major infections of burns dre with the ventilation plant running, and apprecia reduces minor infections This evidence, too, is kno to the surgical staff

What action then could these surgeons take on t evidence ? We made several attempts to minimise flow of contaminated air to the theatres , we re desig the facilities of the sterilisation service, and the flow clean trolleys to clean theatres and the disposal of d material away from the theatre, in an endeavour increase the ease of work and the efficiency of the thea staff as a whole These attempts were not successful preventing operating theatre infection

We are now of the opinion that a radical re design of our operating-theatres is essential to lessen the kno risk of airborne contamination, and this for the follow reasons

1 The dust of hospital wards and corridors inevita contains more bacteria than that of a normal building , despite most careful cleansing precautions, this must alw be so

2 The operating theatre suite is almost always within hospital building, sharing the air and dust of that building

3 *With some types of ventilation in operating theat (such as ours) air is sucked from the hospital building it and drawn into the theatre suite,* thus ensuring the maxim contamination of the operating theatre air

The ventilation plant of all operating-theatres, the fore, needs to fulfil certain requirements

1 The source of air should be above hospital level so as avoid contamination from the air of the hospital a incidentally, from the street The air inlet on the roof of Accident Hospital has proved satisfactory to the Burns U installation

2 The flow of air to the theatre should be such as to prov up to 20 complete changes per hour

3 Filtration of the incoming air is necessary to remove a soot or bacteria-carrying particles

4 The temperature and humidity of the incoming air sho be automatically controlled, both for the comfort of patient and staff and to minimise anæsthetic explosion ri A temperature of about 70°F and relative humidity of 6 is satisfactory for these purposes

5 Since the exhaust air from such a theatre is potentia contaminated it is necessary to remove it to the exterior T must be done without inducing a negative pressure, wh would draw in hospital air from the corridors Similar c siderations make air locks desirable for patients, staff, materials to pass in and out of the air conditioned section.

6 Since preparation work involves steaming sterilis separate ventilation of rooms doing this work is need preferably with an input of the same filtered air that is suppl to the theatres and an independent output carrying the ste laden air to the exterior It is important that air potenti

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1 Sevitt, S *Lancet*, 1949, ii 1075

amminated by passage through the theatre should not be lied to preparation rooms, since this may cause con nation of instruments and equipment to be used for the or subsequent patients

rom this evidence it is obvious that surgeons alone ot meet this quite formidable engineering challenge. the matter does not end there. Since this method entilation is only an additional precaution against ating room infection, the lay out and design of the tre suite must provide the usual aseptic and antiseptic autions against infection. The emphasis now is on a air; therefore a revision of the detail of operating tre lay-out and design is essential on two counts:

All sources of dust collection must be radically eliminated
The maintenance and physical cleansing of all equipment ne normal theatre maintenance staff must be easy—even a complicated problem than it is now

the elimination of all sources of dust collection, no pment can be allowed to hang from the operating tre ceiling For example the present umbrella ed high power theatre lamp hanging immediately re the operating table is often tilted during an ation; and with positive-pressure ceiling ventilation lean air this would result in the immediate con mination of the operation wound with the dust from top of the lamp

addition, all equipment—tables trolleys, and so -that is too big for autoclave sterilisation should be nly designed for ease of washing or spraying with a able antiseptic and wiping down, and such articles ld have no shelf near floor level The ceiling, walls, floor must also be cleanly designed and have no ks or crevices in which dust can collect. Here, then, hospital architect s problem

n adequate source of lighting is essential to all ations, accordingly lighting presents particular blems when it is accepted as a principle that all ting must be *behind* the cleanly designed non-dust- ecting ceilings or walls Thus, involving high quality face and depth lighting of the operation field as well good general lighting, is a major problem for the ting experts.

ster was aware of all these needs for theatre cleanli , and met them as best he could, as have all surgeons e his day Now, however, with our increased know e the task is beyond any surgeon s ability to answer m. The Birmingham Regional Hospital Board has pted the need for a small and closely knit team of pital architects, engineers, and lighting and air ditioning experts to work with a surgeon to meet the ny-sided aspects of this matter The group has rted work and see no reason why operating theatres ld not be quite safe from any major infection; and, thin the bounds of human failings, minor infections ld be considerably reduced.

Your leader states that the essential clean-air plant d I believe we have the only one in the country) ' is pensive to put in and to run.' Our experience in the of this plant is that its capital cost was small and was turned within two years by the considerable reduction wound infection that it effects. The plant is easy and eap to run; the only maintenance necessary is a thly change of inexpensive filters and the running of a horse-power motor In the past eight years it has en used daily without any major breakdown. Any dern operating theatre is costly to build and the dition of a clean-air plant, though adding slightly to e expense, could not be seriously objected to in view its proved usefulness.

Dr Sevitt has recorded the tragedies of 3 major wound ections—an incidence of 0 03% of all patients operated over the period of his inquiry He has not recorded more common minor and trivial infections yet these known to increase significantly the period of inpatient treatment for the patient, and to add to the risks of cross infection in the ward in which he is nursed.

Wound infection of any type is an *expensive* complication From a purely economic aspect, it is always cheaper to prevent than to cure

Birmingham Accident Hospital. WILLIAM GISSANE

SIR,—In his discussion last week of the possible sources of infection in a case of gas gangrene developing after operation on a closed fracture Dr Sevitt says: "Since the original fracture was closed the leg muscles are unlikely to have been contaminated by *Cl welchii* before the operation on the ankle " I was most interested to read this because I have recently treated three cases of gas-gangrene in patients with closed fractures.

Case 1 was a young boy seen four days after receiving a third degree abduction external rotation fracture of the ankle The ankle was grossly swollen and fracture blisters were present The skin was however intact Two days after admission he had developed gas gangrene and below knee amputation was performed

Case 2 was a man with a spiral fracture of the shaft of the humerus, who attended seven days after injury There was no breach of the skin, but he had gangrene of the arm and gas bubbles could be felt over an area extending from the mastoid process to the iliac crest and from the sternum to the vertebral column. The arm was amputated through the shoulder joint

Case 3 was a man with a closed fracture of the shafts of the tibia and fibula. When he came under my care seven days after injury he had gas-gangrene extending as high as the knee Above-knee amputation was performed.

These patients were seen in the Sudan in 1951 and 1952 Before seeing them I was quite ignorant of the possibility of gas gangrene developing in the absence of a wound of some sort, but senior members of the staff of the medical faculty of the University College of Khartoum to whom I turned for advice told me that such cases are by no means uncommon in the Middle East

Newcastle upon Tyne P R R CLARKE

SIR,—In about July, 1917, Mr W McAdam Eccles was distressed by a series of infected wounds in his habitually clean cases. The bacteriologist (the late Dr Canti) placed a number of open petri dishes on the operating table and switched on the ventilating fan. A variety of organisms were sucked under the door from the mat outside and were demonstrated by culture. Since a war was in progress use of the ventilating fan was stopped and we endured the heat I think that this particular theatre was abandoned or replaced after I left the hospital.

Newland, Sherborne
Dorset. JOHN WHITTINGDALE

HYPOTHERMIA

SIR,—In the article on surface cooling by Churchill Davidson et al (Nov 14) and in subsequent correspondence (Nov 21) there has been a notable omission of any reference to the indisputable fact that a generalised and highly efficient response to cold exists in the non hibernating warm blood animal when subjected to any form of surface chilling That this response involves initial increases in heat production and oxygen requirement is well established and only by imposing the added risks of heavy sedation, deep anaesthesia and muscle-relaxing drugs can this calorigenic reaction be even partially inhibited and hypothermia obtained Even under these conditions, while surface tissues are reduced to levels of cold that may cause permanent damage, deeper tissues may not be equally cooled and consequently thermal gradients are likely to arise within the body These have been shown to have among other disadvantages that of increasing the incidence of cardiac arrhythmias. Other undesirable changes occur as the result of surface cooling, including a lowered circulating lood volume, hæmo concentration, increased blood iscosity, hyperglycæmia, eosinopenia, and depletion f adrenocortical lipids and ascorbic acid This widespread physiological upheaval is not seen when hypothermia is induced by cooling the exteriorised circulation,[1] nor has death or tissue injury followed in over 100 experiments in dogs The method requires only the lightest anæsthesia, and premedication and muscle relaxants are unnecessary Hæmodynamic disturbance does not result from the arteriovenous shunt due to a balanced resistance in the exteriorised circuit Despite reports of successful application of surface cooling in relatively small numbers of cases, the accumulated experience in both clinical and laboratory trials has been that this procedure is hazardous and associated with a considerable mortality

A more complete understanding of what has been called "cold stress"—a complex physiological derangement known to follow surface chilling—should be sought before the method is proposed for further clinical trial In infants and children, the greater surface area relative to body mass and the poorly developed heat-regulating mechanism may, as suggested in your leading article of Nov 14, make surface cooling in children a safe and effective procedure

E J DELORME

Department of Surgery
University of Edinburgh

INCISION FOR ACUTE APPENDICITIS

SIR,—Mr Ewing and Mr Monro (Oct. 24) severely criticise the use of the paramedian incision in acute appendicitis Their criticism may or may not be valid, but they certainly do not make their point by quoting a solitary clinical history which could well be misinterpreted as suggesting that this particular patient had inadequate surgery or anæsthesia or both. Mr Shemilt (Oct 31) is similarly dogmatic about the absolute contra-indication to drainage following appendicectomy, but he does not attempt to justify his statement by arbitrarily selected case records

Experience in emergency surgery has convinced me that the average "early" acute appendix can be removed with entirely satisfactory results by any competent senior house surgeon through any standard incision, of which the muscle-splitting is one of the better ones The case which most tests our judgment and skill is the advanced one with perforation or gangrene, in which fæcopurulent exudate is insecurely localised within a barrier of lightly adherent gut and omentum Here the objective should be to approach the area directly through an adequate incision, guard its delicate margins with moist packs, and remove the appendix under direct vision and with careful suction control Fortunately the majority of these cases show maximum tenderness and splinting laterally in the right iliac fossa, and in most of them a mass can be felt in this region when the patient is anæsthetised In these circumstances, no surgeon in his right mind would employ an incision other than one in the right iliac fossa, and my own preference is for the ample exposure offered by the oblique muscle-cutting approach of Rutherford Morison Other surgeons, more skilful or with many powerful assistants, may achieve similar access with MacBurney's incision

But there remains a significant group in which the severely inflamed appendix hangs down into the midline cavity of the true pelvis, or in which it runs upwards and medially among the terminal loops of ileum Here, if the appendix is long and is gangrenous at its tip, the pathological epicentre may lie far from MacBurney's point. These cases can be recognised clinically, and the principles stated above dictate that the appendix should exposed directly by a paramedian incision rather than dragged out by the heels throug Drainage, if desired, can be achieved through a stab incision near the anterior superior spine, and to the iliac vessels or any other structure, from a of supple corrugated rubber so placed and soon remo is non-existent The right paramedian incision is ad tageous also in certain cases of diagnostic doubt, inclu advanced general peritonitis of uncertain though pr ably appendiceal origin. We should use it wh indicated, and should not be discouraged because operators find difficulty in coping with the bowels closing the wound securely

Finally, I envy Mr Shemilt his faith in the invin of the peritoneum, but since there are so many variab statistical proof is lacking Where the appendix shows florid sloughs, severe inflammation, and fæcal contamination I shall continue—I believe, ally—to drain it

E. G. HAR

Baylor University College
of Medicine,
Houston, Texas.

LUNG LESIONS IN ARTHRITIS

SIR,—Your leading article of Nov 21 raises the tion of the ætiology of the nodular lesions descr rheumatoid arthritis by Caplan,[1] who is quot identifying tubercle bacilli in the fibrous tissue, lesions in three fatal cases Reference to the article, however, reveals that tubercle bacill isolated in only one of these cases Furtherm reader is left in considerable doubt about the ex of lesion from which the organisms were obtain patient (case 38) is described as showing, o examination, "progressive massive fibrosis in zones," and at necropsy "masses at the bases of the upper lobes" and microscopically "undifferen fibrous tissue in the masses" The tubercle bacilli obtained "on culture of material from a massive lesio It is also difficult to correlate the radiological with morbid anatomical and histological appearances remaining two fatal cases

Caplan prefers the theory that the lesions he descr in the radiographs ("round opacities") are bas tuberculous to the idea that they are "rheum granulomata" resembling the subcutaneous no histologically In this respect he has the suppo most workers who have studied the lungs in fatal of rheumatoid arthritis. My own experience of 7 cases of the disease is in agreement with the that no specific lesion occurs However, there is su resemblance between the histological appearance rheumatoid subcutaneous nodule and that of caseous tuberculous foci to suggest that, if one mak allowance for the different situations in which the lesions are found, their differentiation might well be difficult matter, should they both occur in the lung There is no question that Caplan's patients presented unusual radiological appearance, but the theory that "rounded opacities" are tuberculous seems, at p to rest upon the demonstration of tubercle bacilli i lesion whose exact nature is not clearly defined tuberculous lesions were present in the lungs of the two cases does not help to establish the opacities" as tuberculous

If the true nature of these fascinating lesions is discovered, it is essential that the terminology u describe their radiological, macroscopic, and histo appearances should be unequivocal Histological nation should not be considered the final st each lesion so examined should be submitted bacteriological investigation

BRUCE CRUICKS

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[1] Delorme E J *Lancet*, 1952, ii, 914

[1] Caplan, A. *Thorax*, 1953, 8, 29

GASTRIC RESECTION

SIR,—In my letter of Nov 7 I referred to an old method used by Rovsing in dealing with gastroduodenal hæmorrhage. I have since seen Rovsing's original communication. He described the method as follows:

> "A gastroscope constructed in principle as the usual cystoscope but of a size corresponding to Charrière no 30–40 is used. It carries a strong lamp and is provided with a canal which is connected to an insufflator
>
> At operation, a small incision is made in the middle of the anterior surface of the stomach, 2 cm. above the greater curvature just large enough to allow the instrument to pass. A purse-string suture is then superfluous. The stomach is pumped full of air until all mucosal folds have disappeared In the darkened room every detail can now be seen in the stomach as well as in the proximal duodenum. Observation of the posterior surface of the stomach is made possible by turning up the omentum and transverse colon Suspicious features can be inspected directly through the instrument which yields much more reliable information than can be obtained by *direct inspection of the opened stomach.*
>
> The method is valuable in differentiating between ulcer and tumour; the extent of a malignant infiltration can be judged with great accuracy Retrograde dilatation of the œsophagus is made easier as the bougie is introduced easily under direct vision.
>
> Its greatest value however, lies in the possibility of detecting quickly small bleeding ulcers which have not been successfully located by any other means. In 4 cases a dark *spot* was seen in the anterior stomach wall. An artery was coursing towards it, to be suddenly interrupted. It was now possible to attack the bleeding point directly ligating it from the outside by means of a stitch going through all layers and reinforcing this with one or two sero serous sutures. The method would be equally applicable to duodenal ulcers of the anterior wall."

It seems that the *short-circuit accident* which I mentioned was the result of connecting the lamp to the mains supply In subsequent cases, a battery was used.

Berne, Switzerland. P LUNDSGAARD HANSEN

GOUT

SIR,—Dr Marson's reply (Nov 21) to my letter about sodium salicylate *therapy* requires a few comments

I was sorry that he was unable to see my more detailed report [1] on uric acid excretion to which I referred because although this showed rises in the serum uric acid levels in the three-day rest after the four days of therapy the rises were moderate On the average a rise from a level of about 2 0 mg per 100 ml. to about 4·0 mg per 100 ml occurred, but occasionally the level continued to fall or remained steady The only acute attack of gout which I saw during my tests took place actually in an interval of rest from therapy in which the serum uric acid did not rise Dr Marson's figs. 3 4, and 5 show serum-uric-acid fluctuations on continuous therapy no less than those which I found in interval therapy, and his cases also had acute attacks during treatment That Bauer and Klemperer's results [2] were *less* satisfactory than mine does not surprise me, because in their trial they used aspirin, a drug whose inferiority to sodium salicylate is commented on by Dr Marson in his paper. The interval therapy with sodium salicylate as described [3] is, incidentally not so much more than sixteen years old, as Dr Marson seems to think.

I can only say that Dr Marson's belief that an initial dose of sodium salicylate sufficient to cause appreciable lowering of the serum uric acid also usually causes salicylism does not fit in with my experience in the treatment of gout and rheumatism with this drug

Dr Marson tells us that he does not yet know how long his strict regimen should be imposed and as Bauer and Klemperer also remark, our evaluation of such treatment must come from clinical results over a long period, and not be based on serum uric-acid estimations It is evident that sometimes with such prolonged treatment the patients themselves must first cry "enough" but with such a potentially painful and crippling disease there should be many who will persevere with the new method If it is found superior to the older interval therapy, then, next after the martyrs to gout, I shall be the most delighted

Edgware General Hospital,
Middlesex. G H JENNINGS

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[1] M D Thesis, Cambridge 1938

[2] Bauer W., Klemperer F *New Engl. J Med.* 1944 231 681

[3] Rep. chron. rheum. *Dis* 1937 2 106

THE INSULIN MYTH

SIR,—It is with commendable courage that Dr Bourne (Nov 7) has exposed the myth. Yet like all iconoclasts he must be prepared to be attacked in turn Loins will undoubtedly be girded It therefore behoves us, who feel that he has said something which has long required saying to come to his defence

The fallacy of insulin therapy lies not in the treatment itself, but in the diagnosis of schizophrenia. Bleuler's concept of schizophrenia was a protest against the prognostic pessimism implied by Kraepelin's dementia præcox Bleuler included in his schizophrenic group many conditions which have never been shown satisfactorily to have any real ætiological relation to dementia præcox or, as it is usual to term it nowadays "process schizophrenia"

Within seven years of the origin of the concept of schizophrenia its unsatisfactory nature became apparent Anyone who wishes to verify this can turn to the *American Journal of Insanity* for 1918—to a paper [1] by Phyllis Greenacre which is as apposite today as when it was written One would have thought that the many excellent studies which have appeared since then such as those of Kasanin and Langfeldt, would by now have had some penetrating effect. These studies, describing "schizo affective" and "schizophreniform" states have shown that a fairly clear distinction can be made between "process" and "benign" schizophrenia although borderline cases can certainly occur

I have myself described these benign schizophrenias as "atypical depressions" and I set out the reasons for doing so [2] The 16 cases in that group which would certainly have been diagnosed as "schizophrenia" by other psychiatrists and indeed in some cases were, have now been followed up over a period of five years They were all treated symptomatically or with E.C.T in no case was insulin-coma therapy administered It is hoped to publish this follow up study in the near future, but it can be said of the 10 surviving cases in which full information has been obtained 5 have remained completely well since their discharge, and 5 have relapsed but responded to further courses of E C T Some of these cases have had repeated episodes of this kind over periods as long as twenty years, but the essential feature is that they do not dement and they are absolutely normal in between 2 of the younger patients having their first attack, and who responded to E C T have both remained well and have successfully undertaken training courses for professional careers since their discharge from hospital

Insulin coma is a prolonged and dangerous form of therapy Its continued use would only be justified if it was shown conclusively to have a curative or at least an arresting *effect in true schizophrenic conditions.* This has never been scientifically proved, and indeed all the evidence is that the cures in insulin-coma therapy are in those very cases which have within themselves the potentiality for cure or which respond to physically less harmful forms of treatment, such as E C T

It is obvious that clear clinical thinking in psychiatry especially on this point, is long overdue if we are to appreciate fully the value of the different forms of physical treatment which are now so freely used Schizophrenia is not a disease but a congeries of different conditions, the natural history of these conditions must be studied more closely if we are to see which are benign and which are malignant. In exposing the insulin myth, Dr Bourne has indicated the way

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[1] Greenacre P *Amer J Insan* 1918 75, 197

[2] Jarvie H. F *J ment Sci.* 1950 96, 203

Department of Neurology,
Radcliffe Infirmary,
Oxford
HUGH F JARVIE

SIR,—Dr Bourne has shown that, by selecting one kind of evidence and disregarding another, he can convincingly prove to himself what he has set out to prove

I have applied hypoglycæmic treatment to 1300 schizophrenic patients of both sexes, and E C T to many hundreds of others, in the treatment centre at Springfield Hospital since 1940 (I am excluding schizophrenics treated at other hospitals since 1936) This group of 1300 patients constitutes a homogeneous series as regards diagnosis, prognostic criteria, and assessment of degrees of recovery It has also been subjected to a "follow up" over a long period

The course of treatment I apply consists of 50–60 deep comas in each case, divided into six weekly coma doses E C T has been given in most cases in conjunction with insulin and has proved its value But E C T alone is without much effect, any improvement noted being transitory, no matter how many times or at what intervals E C T was given

Obviously it is essential to compare comparables only, and it is clinically and statistically quite unsound to add the results of such treatment, as applied in many hospitals, to the results of "diluted" hypoglycæmic treatment—as with subcomas, short comas, reduced number of comas, and so on—and to draw conclusions from this Many accounts disregard this point

To administer E C T alone to a schizophrenic, if there is no contra-indication to insulin, is to deprive the patient of a reasonable prospect of recovery

In my series every precaution was taken, in assessing results, that my judgment should not be disturbed by expectations gloomy or optimistic My experience has revealed to me that although hypoglycæmic treatment, combined with some E C T and followed by psychological rehabilitation, is far from the last word in the therapy of schizophrenia, it is at present the best we can offer Because of the unsatisfactory state of our concept and knowledge of schizophrenic illness in all its forms, all physical treatments are applied faute de mieux

Although reports and reviews of hypoglycæmic treatment and E C T in schizophrenia abound in this country and abroad, I support Dr Sandison's suggestion (Nov 21) that a committee of the R M P A should be instituted to review hypoglycæmic treatment in our hospitals

London W 1
CHARLES FRIEDMAN

SIR,—Certainly at least one side of Dr Bourne's contention that insulin treatment of schizophrenia has only mythological efficacy is belied by the observation every psychiatrist will have made occasionally As soon as the patient who may have been quite refractory to any other treatment starts his comas, he loses some of his symptoms That this is not merely due to the increased attention, to suggestive factors working on patient or therapist, or to chance, is clear to anyone who sees as often as I do the changes for the better in patients who, for one reason or another, have gone through a more than usually protracted period during which only sopor was attained This applies in my experience equally to patients who have had previous E C T, concomitant E C T, or none at all

Whiterton Hospital
co Durham
D J SALFIELD

PROLONGED APNŒA FOLLOWING SUCCINYLDICHOLINE

SIR,—Undoubtedly, all cases of sensitivity t succinyldicholine should be published, especially wh they are due to rare conditions such as the greatly reduced pseudocholinesterase level in a normal subje described by Dr Forbat and his colleagues (Nov 21 However, I criticise the dose of 50 mg of 'Scoline for a cystoscopy and examination under anæsthe which in fact was completed in five minutes. Seve published cases of inconvenient prolongation of eff have followed administration of 50–100 mg, and it unfortunate that such doses are still recommended f similar procedures, and are widely quoted by the man facturers Smaller doses, which can always be supple mented when necessary, would avoid such unexpe incidents

The individual variations in response to the drug a great. In a series of 350 abdominal operations, using th continuous drip technique for relaxation, I have fou that the average maintenance dose of succinyldichol is 300 mg per hour. However, doses as high as 1100 m per hour have been needed on occasions, and in cert patients with subnormal pseudocholinesterase lev 60 mg per hour was adequate for full relaxation The fore, the administration of such unnecessarily lar initial doses as those recommended cannot be justified

The wide variations in response, associated with th occurrence of abnormal pseudocholinesterase leve does not contra-indicate the use of succinyldicholi provided the administration is on a rational bas In practice, the flexible controlled relaxation that can produce is invaluable, and it would be regrettab if the publication of incidents of avoidable overdo should retard a great advance in anæsthesia. T use of test doses in many cases reported would hav reduced them to academic and biochemical, rather th clinical, significance

Portsmouth
R J HAMER HODGES

VISITING CHILDREN IN HOSPITAL

SIR,—There seems to be a lamentable tendency the days to regard children as so many bundles of psycho logical problems—a tendency followed, no doubt with excellent intentions, by your annotation Having don some children's nursing I have seen the problem fro both sides, and my sympathies lie with the children an their parents by all means let us have visiting of th children as often as possible—preferably daily Let u not, however, search too hard for complex psychologica reasons for visiting, nor attribute to lack of it too man undesirable childish habits One does not have to be psychologist to know that a child wants and needs it mother—an unnatural child of an unnatural mother th does not! But a good many mothers who have suffere embarrassing moments from childish outspokenness an inability to dissemble feelings may ask how it is prov that a child inwardly pining and miserable is "capab of interest and animation on the surface" On the who the comments of the young East-enders leave one in litt doubt as to their feelings on entering, staying in, an leaving, hospital Your annotation counsels the docto opposing the daily visiting of children against trustin their own observations "which investigation has prov to be misleading" May we know whose observation ha shown "bed wetting, temper tantrums, delinquency an the like" to be attributable to a stay in hospital, an what steps were taken to ensure that *such* observation not misleading too? Does boarding school produ similar symptoms, demanding daily visiting also?

There are plenty of excellent reasons for allowin children to see their parents every day in hospital, with plea for discretion where necessary, on the part of bot hospital staff and parents, not the least reason being the growth of confidence in the hospital on the parent's part and increased experience and understanding of the parents on the part of the nursing staff It is not needful to create added complexities in the unfortunate children

Colchester JEAN PENFOLD

*** We would like to refer Mrs Penfold to the evidence cited by Dr Ronald Mac Keith (*Lancet*, Oct 24 p 843) to Dr John Bowlby's monograph *Maternal Care and Mental Health* (W H O Monograph Series no 2) and to the film 'A Two-Year Old goes to Hospital.'—ED L

IDENTIFICATION OF PILLS

SIR,—A year ago Dr Russell and Dr Thorne[1] described a tablet-identification box, and their article was followed by some correspondence on this subject

It seemed to me then that much uncertainty could be removed—both in the treatment of overdosage and in general practice—if we all got into the habit of putting the name and dosage of each drug on its container I started to write this in full under the Sig part of each prescription until I discovered from a friendly chemist that all one need do was to write *Nomen proprium* (shortened to Nom. prop) with the instructions to be put on the container The dispenser then puts the description and dosage on the packet

I have now been doing this for some months and find it a great help, both to my own brain which does not have to recall whether the white tablets for Mrs. Jones's breathlessness are phenobarbitone, digoxin, aminophylline, ephedrine, or anything else and to my partners who no longer have to recall which is my favourite sedative or *carminative when it is demanded as a repeat* by one of my patients.

I may say that, in our firm, opinions are strongly divided one colleague is enthusiastic and has written to our local hospitals asking that their dispensers do the same for consultants occasionally alter treatments in patients who attend over long periods, without our being aware of the change Another colleague feels that knowing exactly what they are given may make the more sophisticated patients introspective or distrustful—that a little faith helps a lot—or that they may tend to prescribe for themselves.

Totton, Southampton EOIN L. MCQUITTY

SALMONELLÆ IN TORTOISES

SIR,—Boycott et al[2] state in their article on salmonella in tortoises, mentioned in your annotation of Aug 15 that 'no-one to our knowledge has examined the fæcal flora of *Test græca* in its native haunts.'

We started such an investigation in March 1953 going back to a casual observation in 1930 which could not at that time be followed up systematically Our findings will be published in due course. The following results have so far been obtained

A high proportion of free-living healthy tortoises of the species *Test græca* (syn. *ibera*) in *Palestine are salmonella* carriers, not so rarely harbouring in their bowels more than one type It may be assumed that, once naturally infected, a tortoise remains a carrier of salmonellæ for the rest of its very long life. It is known that *Test græca*—the swine among the reptiles, as it has been called—is an omnivorous animal feeding even on mammal excrements. Therefore if Boycott et al. make the suggestion that 'the high carrier rate of salmonella in imported tortoises may be due to infection in transit," they are right in being 'not convinced that this is the entire explanation.' As for the rest we can confirm that the salmonellæ these tortoises are excreting belong to the new types or are types not hitherto described.

Moreover we do not know if human infections have been caused by keeping tortoises as pets. Nevertheless the warning of Boycott et al regarding the risk to children should be taken to heart, all the more so because, contrary to the experience of these authors, we found that production of fæces was not so infrequent and that they were soft and relatively voluminous if fresh vegetables were given as food

Central Laboratory
Workers Sick Fund (Kupat Holim)
Haifa, Israel

WILLY HIRSCH
RAJA SAPIRO HIRSCH

CORONARY HEART DISEASE AND PHYSICAL ACTIVITY OF WORK

SIR,—Dr Morris and his collaborators have put forward a very interesting hypothesis and have been to great pains, with I think some success, to show that the excess mortality amongst sedentary workers is not due to their social circumstances—i e their income, which implies the amount of money available to spend on food, particularly the most expensive article of diet fat.

That this was a major hazard to surmount is obvious in that most work that requires physical activity is paid at a lower rate than work which can be done from a desk I trust that their exposition will not draw attention from the fact that the main factor in the pathogenesis of atherosclerosis and hence coronary disease is a disturbance of cholesterol metabolism and in case your readers have not yet read it, I would like to draw attention to a recent article by Ancel Keys[1] which is a fascinating addition to the vast literature already available on this matter Keys states that American males aged 40–65 have a higher mortality rate than males in any other major country excepting only Japan and Portugal This high mortality was found to be due entirely to *heart-disease mainly coronary heart-disease Americans* according to Keys have the highest fat consumption in the world and the cholesterol blood pictures in these men are in line with this argument Keys also mentions this fact of physical activity in the ætiology

I have always felt that there is one other factor involved in the deposition of cholesterol in the elastic arteries—first suggested by Thoma nearly sixty years ago—and that is a relative slowing of the blood-stream When the lipophage was incriminated by Leary I brought forward evidence,[2] to show that by the application of simple physical data it could be shown that this deposition occurred in elastic arteries where the blood velocity was slowest The lipophage theory is out of date now but I wonder if similar considerations could not apply to the modern lipoprotein macromolecules or the chylomicrons. If this is the case may we assume that there is a faster blood flow in the main coronary arteries of those whose work involves physical labour and hence their relative immunity to cholesterol deposition?

Ilford. I GORDON

SIR,—I am most interested in the statistical analysis by Dr Morris and his colleagues, and in your leading article last week *In a recent article*[3] *I anticipated* your conclusions that the increased incidence of coronary heart-disease in general practitioners is due to lack of exercise and sedentary conditions and that the higher incidence in the professional and upper classes may be *also due to the richer diet in these classes.*

When Morris et al[4] in their study of 6000 records of medical practitioners showed that the incidence of coronary-artery disease was greater in general practitioners than in specialists and other doctors, I came to the conclusion that this was due to the lack of exercise owing to the general practitioner's hours of work most his time being spent sitting at his desk doing his argery, or sitting at the wheel of his car visiting patients Having practised both as a general practitioner and as a specialist for many years, I could not accept the view that the mental stress of a specialist today was any less than that of a general practitioner

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[1] Russell, B., Thorne, N A *Lancet* 1952, ii 1254
[2] Boycott, J A., Taylor J Douglas, S H. *J Path. Bact.* 1953, [illegible]

[1] *Amer J Publ. Hlth.* 1953 43 1399
[2] *Arch. Path.* 1947 44 247
[3] *Med Pr* 1953 230 533
[4] Morris, J N Heady J A., Barley R. G *Brit. med J* 1952 i, 503.

As you point out, there are two problems to consider—the causes of the basic atheroma, and the causes that lead to occlusion Recent work, particularly by Gofman,[5] has shown that atheroma is related in some way to lipoid metabolism, and according to Gofman the recurrence-rate of myocardial infarction is significantly lessened in patients with established coronary artery disease whose level of lipoproteins has been reduced by estriction of dietery fat Genetic influences, however, must play an important part, and in some cases are probably more important than habits of life and work, for how otherwise can we explain the advanced degenerative atheromatous lesions found in the coronary arteries at an early age, which I found to exist in a review of 100 cases of coronary occlusion in young adults.[6] Most of these young patients would have fallen into the Registrar-General's social classes IV or V There was no indication that special stress had been a sustained experience

Nevertheless, as I have pointed out,[3] even if an individual is hereditarily predisposed to atheroma the incidence of could be made by the general practitioner

" A useful contribution to the lowering of the incidence of coronary occlusion could be made by the general practitioner Patients who have a family history of coronary disease or hypertension and particularly if they are of the coronary physique (mesomorphic type) should be advised to regulate their diet particularly as regards the lipoids so as to avoid overweight and obesity If the occupation is of a sedentary nature regular exercise should be taken. The practitioner himself should also note the saying 'Physician, heal thyself' "

MAURICE NEWMAN

Blackpool.

ARTERIAL TRANSFUSION

SIR,—I was delighted to read Dr Allan Brown's experiences (Oct. 10) with arterial transfusion and bleeding in neurosurgery I have seen how smoothly and efficiently this can be performed with a closed circuit apparatus as designed and used by Dr Peter Mortimer of the Bristol Neurosurgical Unit[7]

I am prompted to report a case in which arterial transfusion was used for resuscitation, as the response dramatic, though not maintained because of con- ed hæmorrhage

A man of 53, who had been run over by a bus, was seen 6 30 P M on Oct 13, 1953 He was unconscious and verely shocked with a fractured pelvis, open fractures of e right leg and left ankle, right mid thigh and supra ondylar fractures, and a possible fracture of the base of the skull The muscles of the right calf were extensively denuded. Resuscitation in the ward with dextran and blood intravenously produced temporary improvement The maximum blood pressure was 110/75 mm Hg, and the pulse-rate was 84 at 7 P.M There was no further improvement

He was given atropine gr $^1/_{100}$ and was taken to the anæsthetic room in his bed at 9 45 P.M A rapid decline was noted The intravenous blood transfusion would not run Respiration was slow and periodic, there was extreme pallor and a relaxed jaw A laryngoscope was used to expose the relaxed ds which were sprayed with 2% amethocaine A cuffed be was passed easily Assisted respiraton with oxygen ought some colour back and a faint radial pulse The atient was transferred from the bed to the operating table hich was in a 20° Trendelenburg position.

The surgeon cut down on the right femoral artery, and transfusion by this route was started at 10 P.M. Four pints of blood was given in forty minutes. The respiration rate improved dramatically to 30 or 40 per min, and the systolic pressure rose to 80 mm The peripheral circulation of ears and nail beds improved and the intravenous transfusion began to run well An anæsthetic consisting of ga oxygen (2:1), pethidine, and 'Scoline' (50 mg of was given. A right mid-thigh amputation was pe A suprapubic incision revealed extensive extrape bleeding and blood-clot, a ruptured urethra, and vasated urine The bladder was drained. The bleeding could not be arrested and packs were inserted

At midnight the patient was returned to the ward left the theatre with a systolic pressure of 70 mm tracheal oxygen was continued The blood pressure re at about this level during the night The pulse-rate 120, and the lungs were dry, but he deteriorated and at 6.15 A.M. The total amount of blood given was pints, and of dextran six pints.

At necropsy extraperitoneal extravasated blood from pelvis had extended to the lower poles of the kidneys was a fracture in the base of the skull and a small su hæmatoma. Although these injuries were "not comp with life," resuscitation did enable the amputation exploration of pelvis to be performed.

R. D. Le

Central Middlesex Hospital,
London, N W 10

THE LETHAL AEROSOL

SIR,—It came as a surprise to me recently to that seasonal pollution by smoke of the air of L was already becoming sufficiently troublesome in days of Harvey to be regarded by him as a poten cause of disease

On Nov 14, 1635, there died in London, at the age of 152 years, Thomas Parr, a native of Shrop who had been brought from the country and presen to the King as a natural curiosity A dissection of body was performed by Harvey, from whose re the following passage is taken

" The cause of death seemed fairly referrible to a change in the non naturals, the chief mischief being co with the change of air, which through the whole course of had been inhaled of perfect purity—light, cool, and mo whereby the præcordia and lungs were more freely ventila and cooled, but in this great advantage, in this cherisher of life this city is especially destitute, a city grand characteristic is an immense concourse of men animals, and where ditches abound, and filth and offa scattered about, *to say nothing of the smoke engendered by general use of sulphureous coal as fuel, whereby the air is times rendered heavy, but more so in the autumn than other season.* Such an atmosphere could not have been otherwise than insalubrious to one coming from the sunny, and healthy region of Salop, it must have especially so to one already aged and infirm " (My itali

This is one context in which antiquity does not hal On the contrary our discredit is the greater in tha are shown to have been subjecting ourselves to th toxic vapours for so many generations and have no found a constructive solution

G A K. Mi

Department of Pathology,
Guy's Hospital London, S E 1

REPUTATION OF SPINAL ANALGESIA

SIR,—At the hearing described in your issue of No (p 1000) a professor of neurosurgery is reported have stated that an anæsthetist should know tha normal dose of spinal anæsthetic is dangerous involves the risk of permanent injury In the report, a distinguished neurologist asserts that it is time that the whole problem of the complication spinal anæsthesia was re-examined by the medical fession While venturing to question the accura the first opinion as reported, I suggest that nothin good can come of the second suggestion B re-examination must not be prejudged

The neurologist, medical and surgical, sees very rare bad result, just as the laryngologist uncommon granuloma of the vocal cord follow tracheal intubation, the dental surgeon the r a tooth caused by a laryngoscope, the chest physician s unusual severe chest complication following a surgical eration. Is the anaesthetist to be precluded from using s customary methods of anaesthesia because of the rare mplication, when tens of thousands of patients show such complications at all ?

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[5] Gofman, J W *Wis med. J* 1952 51 7 087
[6] *Lancet* 1951 i 1045
[7] Mortimer P L. F *Anæsthesia*, 1951, 6, 125

[1] Harvey William Circulation of the Blood and o
Trans. Willis. London, 1907

It is an unfortunate fact that anaesthesia and analgesia ust always be purchased at a price and every care ust be taken to see that this is the smallest one possible ut, in spite of the greatest care and attention to detail casionally it turns out to be high whichever method technique is used

At the present time most surgeons and anaesthetists ould agree that the indications for spinal analgesia ave greatly decreased since the use of muscle relaxants came general, but I submit that the method when roperly indicated—e.g., in certain obstetric or pelvic perations—and when skilfully carried out, may be of finite benefit to the patient and should not therefore e lightly discarded

Westcliff-on-Sea. J ALFRED LEE

THE ASCENT OF EVEREST

SIR,—The annotation entitled The Ascent of Everest your issue of Nov 14 contains the statement that the 1953 Expedition differed from its predecessors having a physiologist who was not a mountaineer

This statement is incorrect. The physiologist had fact as much mountaineering experience as most of e climbers, but one cannot do physiology and climb well. The scientific contribution to the success of e expedition was made possible by the survey of hysiological problems carried out the previous year n Cho Oyu. This could not have been done by a hysiologist who was not a mountaineer

Medical Research Council Laboratories
London, N.W.3 G PUGH

SUBCLINICAL POLIOMYELITIS INFECTIONS

SIR,—Dr Bradley (Nov 28) is to be congratulated n maintaining his concept of ' narrow stream spread f poliomyelitis in the face of overwhelming torrents of vidence to the contrary

Dr Bradley notes that ' examples of ' narrow stream ' pread have now been recorded by many field workers. ' have not been able to discover any field studies which fter critical examination, alter my belief that polio myelitis virus is *widely* disseminated. The best example of hat Dr Bradley calls limited selective distribution " f virus is probably that of Brown et al.[1] While I do ot wish to embark on a criticism of their paper it eems worth pointing out that the strains of virus in he outbreak which they studied were of low pathogenicity and a single monkey might not have demonstrated virus in a single specimen Tests by a more ensitive technique—e.g that used by Melnick and Ledinko[2]—might well have shown a more widespread distribution of virus Perhaps more important is the point that in studies which have suggested a limited selective distribution there may have been little virus in evidence at the time the samples were taken for virus isolation A serological technique such as that employed by Melnick and Ledinko overcomes this difficulty

It would seem to be short-sighted to base any conclusion of possible control methods on a single study or even a single method of approach The concept of a wide dissemination of virus as opposed to a narrow stream, is reached from epidemiological, as well as serological studies and virus isolations. At the same time, it should be stressed that the much quoted 100 : 1 or 1000 1 ratio of non paralytic to paralytic infections is a cumulative estimate and does not necessarily represent the finding in any one outbreak This ratio probably varies greatly with a number of factors—e g the strain of the virus and also perhaps the habits of the people With regard to the latter it is hoped that Dr Bradley's ' general measures for controlling ' the spread of poliomyelitis will provide some information Control measures have not in the past been employed because presumably, most people are more than doubtful that they would be successful Nevertheless, I think I would share with you Sir, surprise and delight if control methods based on the ' new evidence ' to which Dr Bradley refers are attended with success

London N W 7 G W A DICK

LACTIC ACID IN THE TREATMENT OF OSTEO ARTHRITIS

SIR,—I entirely agree with the criticism of Dr Lawrence's conclusions made by Dr Vergette in your issue of Nov 28

Though I have not found that the intra-articular injection of an acid solution arrests the disease of osteo arthritis, it certainly gives remarkable relief As a result of this Dr Vergette was almost overwhelmed by the large number of patients to whom he gave fortnightly injections The object of this letter is to suggest to Dr Vergette the use of acid potassium phosphate (with procaine) rather than procaine lactic acid Injections have to be given less frequently A fortnight's interval after the first and then injections every four or five weeks will in most cases, maintain the relief

London, W 1 H WARREN CROWE

Parliament

New Industrial Diseases Benefits

THE House of Commons gave a second reading on Nov 23 to the Industrial Diseases (Benefit) Bill. Mr OSBERT PEAKE Minister of Pensions and National Insurance, explained that its main purpose was to extend the provisions of the Pneumoconiosis and Byssinosis Benefit Act, 1951, to cases of partial disablement. The 1951 Act provided compensation for cases of total incapacity or death in people with pneumoconiosis or byssinosis who failed to get benefit or compensation either under the Workmen's Compensation Acts or the Industrial Injuries Scheme which supplanted them in 1948 Since the 1951 Act came into force in March, 1952 some 6000 medical examinations had been made. In the first few weeks the panels had dealt with about 250 cases weekly but the rate had now fallen to about 50 So far, 3300 awards had been made for total disablement and 840 for death. It had been generally agreed that the 1951 Act should, if possible, be extended to cover corresponding cases of partial incapacity, but a formidable difficulty was the immense burden which might be thrown on the medical panels both by a flood of original claims and by the possibility that, as disablement progressed re-examination and re-assessment would be needed The present Bill proposed a flat rate of payment equal to half the rate payable under the 1951 Act for total disablement. This would apply to all cases of partial incapacity of a degree sufficient to attract a continuing payment under the old Workmen's Compensation Acts. This meant that a single medical examination would suffice at any rate until the time when partial incapacity became total Even with this rough and ready method the new scheme might entail nearly as many extra medical examinations as the panels carried out in a single year under the Industrial Injuries Scheme. Clearly these examinations would have to be spread out over a fairly long period, but some people would qualify right away

The reason why the title of the Bill was not the same as that of the 1951 Act, Mr Peake explained was that the Trades Union Congress had brought before the inistry some cases of cancer, including mule-spinner's ncer, and cancers caused by X rays or radioactive bstances, which developed slowly and might exceed he time laid down for making a claim under the Work-nen's Compensation Act, 1925 A general power was being taken in the new Bill to make a scheme for cases of late development. The cost of the proposals embodied in the Bill in a full year were estimated to impose a charge on the Industrial Injuries Fund of £750,000 for pneumoconiosis, and perhaps £50,000 to £60,000 for other diseases.

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[1] Brown G. C., Ainslie, J P., Gilliam, A. G., Zintek, A R., Francis, T jun. *Amer J Hyg* 1952, 55 49

[2] Melnick, J L., Ledinko N *Ibid* 1953 58 207

Clean Food Bill

In the House of Lords on Nov 24, Viscount WOOLTON, Chancellor of the Duchy of Lancaster, moved the second reading of the Food and Drugs Amendment Bill,[1] which he hoped would be known popularly as the Clean Food Bill Lord Woolton said that the 1938 Act, useful as it was, no longer protected the public from either the carelessness or the perfidy of human beings. Since the war the habit of "eating out" had also grown and now extended over a wide range of people and places and prices. There had also been a great increase in the use of food prepared in factories and in the variety of processes of food manufacture. The scientist had become an important factor in food manufacture in recent years and had added much to the convenience and pleasures of life But all the contributions of science were not clear gain In any trade there were some who were careless, some incompetent, and some not too scrupulous. The present laws on adulteration came from a cruder age when the treacherous trader mixed alum with his flour and sand with his brown sugar In our more inventive and complex age, it had become the more necessary to protect the public from those who either from ignorance or greed endangered the public health. The Government were satisfied of the need to regulate these matters and to preserve a balance between what was good in science and what were the dangers The present law had proved particularly inadequate in dealing with chronic toxicity, and the Bill laid down that the cumulative effect of additions or subtractions of ingredients or processes must be taken into account.

But when all was done, Lord Woolton continued, much remained in the hands of the individual trader The individual consumer must enforce higher standards by making more fuss when he met dangerous or disgusting practices

The parts of the Bill which appealed to Lord WEBB-JOHNSON were those designed to deal with misleading labels and advertisements, and those which regulated the addition of specified chemicals It was true that the ublic themselves could do much to impose the adoption f cleanly methods on those who served food But the ublic were often not particularly well informed on the orrect way of handling food, and he hoped that every encouragement would be given to voluntary associations, such as the Order of St John, to extend their courses of instruction on food matters

Lord HADEN-GUEST hoped that the many regulations which would be required by the Bill would be written in plain English so that their purpose would be abundantly clear to those who were to carry out the work of inspection and to keep clean places where food is sold

Lord SEMPILL held that the Bill did not give the Ministers sufficient power to prohibit the use of substances or processes which might have a deleterious effect on health Eminent biologists and medical men had affirmed that the main reason for poor health in this country was the number of toxic elements in food He believed it to be vitally important that the food on our tables should be the natural products, free from the adding and extracting ministrations of the food chemists, and treated with great discretion by the refrigerating and processing technicians

Lord BLEDISLOE said that dispensing chemists were apt to paste their own label over the manufacturers' label when they were dispensing a proprietary preparation n a doctor s prescription This concealed not only the name of the drug but also the formula of its composition Lord WOOLTON thought this practice would be prohibited under the Bill

Drug-supplies for the East

In an adjournment debate on Nov 30, Mr HEATH AMORY, Minister of State for the Board of Tr some drugs, such announced that the controls on some sulphonamides, antibiotics, anti-malarials, and sulphonamides be lifted at the end of this year

QUESTION TIME

Sale of Condemned Meat

Replying to Mr BARNETT JANNER, Major GWILY GEORGE, Minister of Food, said that disposals of con meat and offal by public auction began on Aug 1, 19 during August approximately 1100 tons were sold in

Mr. JANNER In view of the large quantities which are being sold, will the Minister take further cautions than those indicated by him hitherto and see that meat does not reach places where it will be used for h consumption ? Does he realise that the very high p being paid indicate that it is being so used ?—Major GEORGE Under the new conditions of sales certain pr have to be gone through before the meat can be sold furthermore, under the new Food and Drugs Bill gre powers are taken to safeguard the position He hope introduce the new conditions of sale in time for tha auctions in December.

Sodium Fluoride and Dental Decay

Mr. WILLIAM ROSS asked the Secretary of State for Scot in which areas an effort was being made to reduce den decay by the application of solutions of sodium fluo Mr JAMES STUART replied Work of this kind has carried out among school-children in Dundee, Edinburgh, an Fife

Motor-cyclists and Crash-helmets

Mr R W SORENSEN asked the Minister of Transport and Civil Aviation what information he had demonstrating protective value of crash helmets to motor cyclists, whether there was a supply of these helmets sufficient for motor cyclists.—Mr HUGH MOLSON replied, Medical shows that the wearing of the best type of helmet gre reduces the likelihood of fracture of the skull in accidents makes head injuries generally less severe, and sample of taken before crash helmets were common in civilian indicated that the incidence of head injuries in motor accidents was over 50% among civilian riders but only abo 27% among Army riders wearing crash helmets I underst that supplies of crash helmets appear to be keeping pace wi the present demand.

Hertford British Hospital, Paris

Replying to a question, Mr A D DODDS PARKER, Jo Under secretary of State for Foreign Affairs, said that hospital had been shut completely since the summer of 195 In 1951 which was the last complete year in which all departments of the hospital were open and in use, the expenditure on maintenance was 49½ million francs. Dur that year fees paid by patients amounted to 17½ mill francs and income from investments was 4½ million The hospital s total income from all sources was therefo 22½ million francs, leaving an excess of expenditure ov income of 27 million francs (£27,300 approximately) Volun tary gifts during the year amounted to 15½ million francs and the net deficit was therefore 11½ million francs (£11,600 approximately) In 1950 when the cost of maintaining the hospital was only 42 million francs—i e, over 7 million fran less than in 1951—the excess of expenditure over income 18 million francs which was reduced by voluntary gifts subscriptions, amounting to 16 million francs, to a net defi of 2½ million francs (£2,400 approximately)

Tuberculosis Hospitals Waiting-lists

Replying to Brigadier MEDLICOTT, Mr IAIN MACL Minister of Health, said the numbers of patients suffering tuberculosis on the waiting lists for admission to hospita the end of 1950 1951, and 1952, respectively, were 9378, and 6126

Teaching Hospitals

Sir WALDRON SMITHERS asked the Minister of Health changes were contemplated in the policy of administra the teaching hospitals —Mr MACLEOD replied at present

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[1] See *Lancet*, Nov 21, 1953, p 1091

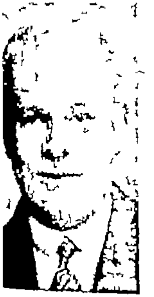
Obituary

BASIL HUGHES

D.S.O., M.A., M.B. Camb., B.Sc. Lond., F.R.C.S.

Mr Hughes, who died in London on Nov. 21 at the e of 75, will be remembered in the North for his work surgeon to the Bradford Municipal General Hospital d by colleagues elsewhere for his work in France and lonika in the 1914–18 war.

He was the son of Captain John Hughes, R.N., who er became a mathematical scholar of St. Catharine's College, Cambridge. From Eastman's R.N. Academy he went to Selwyn College, Cambridge. Perhaps influenced by his father's taste for mathematics, after he took his degree in 1907—he was well up in the list of wranglers—he was for a short time mathematics master in a Shropshire school. He then took up the study of veterinary surgery, but the interest thus aroused in anatomy and physiology made him change to medicine, and he entered King's College Hospital with a scholarship. After a brilliant career as a student he qualified in 1909 and was appointed resident surgical officer at The Hospital for Sick hildren, Great Ormond Street. In 1911 he took the R.C.S. and the same year he became resident surgical ficer at the Bradford Royal Infirmary. Two years later e set up as a consulting surgeon in Bradford.


[Walter Scott

At the outbreak of war in 1914 he was called up at nce as a Territorial officer and after six months in ngland went as a regimental medical officer to France, here most of his time was spent in the front line or e nearest clearing-station. The saga of these years n be read between the lines of his *War Surgery from ying-line to Base*. H. S. B., his collaborator in this ok, recalls the stir and controversy engendered by ughes's work and personality in the Army hospitals in lonika in 1916:

"He came to Salonika from France already endowed ith a unique experience of war surgery in the front line en in the trenches. While there he had made a searching actical study of the technique of irrigation of wounds troduced by Carrel and Dakin, and he had finally discarded e older antiseptic methods in which he had been trained n favour of the new. In Salonika, where no-one had yet actised these methods, he naturally encountered a good al of opposition, not unmixed with professional jealousies ut despite all difficulties his unit in the 28th General ospital soon became a show place for war surgery.

"It must be difficult for younger surgeons to visualise the eatment of war wounds, especially those complicated by s-gangrene and profound shock, without the aid of chemotherapy, antibiotics, or blood transfusion. The patient, after surgical débridement, had to rely solely upon his own owers of recuperation, aided at this time by continuous rigation of the septic surfaces with hypochlorite solution. The first impression one had of Hughes's wards was of a rest of irrigating stands supporting automatic flushing pparatus with rubber tubes stretching out in all directions o the patients in adjoining beds. It was most exhausting ork, not only for Hughes himself but for all his medical nd nursing staff, but it was carried on with great enthusiasm hen much improved results began to be apparent. There ust be many soldiers of that time who were saved from mputation by the skilled and devoted work of Hughes and is teams in Salonika."

Hughes's long sound basic training, combined with his war experiences, turned him into a brilliant surgeon, and his reputation was enhanced by a charming manner and winning ile. He was, however, an intense individualist and could not work long with anyone whose views differed even slightly from his own. There would come a sudden revulsion of feeling as if his Celtic temperament had been jarred, and then an apparently inexplicable coldness and usually final estrangement. So he tended to become a somewhat lonesome figure, pursuing his own brilliantly successful career almost alone.

He lived a long and strenuous life with single-minded devotion to the task upon which his heart was set. That was to give his patients equally, and with right good will, the highest skill which surgery could provide—whether they were Tommies in the trenches, poor children in a Bradford Hospital, or wealthy private patients—and he followed his gleam with zest and fervour and joyful satisfaction.

For his war services the Order of St. Sava of Serbia was conferred on him, and in 1918 he was appointed D.S.O.

After the war Hughes returned to Bradford, where he was appointed assistant surgeon to the Children's Hospital and later to the Royal Infirmary. About this time St. Luke's Hospital was being transformed into one of the great municipal general hospitals of the country, and in 1922 Hughes was appointed one of its first consultant surgeons with 100 beds. Here he found full scope for his operative ability in general surgery.

B. H. S., who was his colleague in this venture, still remembers his first meeting with Hughes soon after he came to Bradford.

"A short lithe figure—he had played in the forward line of the Stoke City A.F.C.—surmounted by a large well shaped head, shy cherubic features, and a philosopher's brow. But it was during our 18 years together at the Bradford Municipal General Hospital that I came to know and appreciate his work.

"He made the surgical side of the hospital known and respected throughout the West Riding and beyond. The hospital's success in its new rôle was largely based on his reputation. To see him operate was an æsthetic delight and a lesson to the ham handed. The theatre hushed as at a solemn rite, his sensitive hands moving delicately, smoothly, swiftly, purposefully through all stages of the operation. He was the first in the North to try out Avertin as a basal anæsthetic. During the latter half of our association he did most of his abdominal surgery under local and splanchnic analgesia. He brought new ideas from Vienna and Denmark on fractures and gastric surgery. His list at St. Luke's often included 15–20 operations. He was a man of restless activity and well-stored mind, and in his meagre spare time he found solace and pleasure in music, of which he was an informed lover and a fine executant on piano and organ."

During the second world war Hughes again did great work for wounded Servicemen and initiated and organised a special ward at St. Luke's for the prevention and treatment of shock. He was a fellow of the Association of Surgeons of Great Britain and Ireland and a founder member of the International College of Surgeons.

When he retired in 1945, he characteristically took up a completely different occupation with great enthusiasm and success. He became a farmer in Cornwall, installed the most up-to-date equipment on his farm, did all his own tractor work up to the age of 75, and lived a hard working country life away from all except local society, as self contained as ever. He became an enthusiast for completely natural home produced food, especially wholemeal bread. "My patients," he wrote to a friend, "are now the population of the soil," and he strove to produce the highest nutrients from the soil with the same enthusiasm as he had striven to help his patients.

Mr Hughes married in 1932, as his second wife, Miss Norah Blaney, the actress, and she survives him.

THOMAS WILLIAM LUMSDEN

M.D. Aberd.

Dr Lumsden, director of cancer research at the London Hospital from 1930 to 1942, died on Nov. 24 at the age of 78.

He was the son of the Rev. Edward Lumsden, of Midmar, Aberdeenshire, and he was educated at Aberdeen Grammar School. At the University of Aberdeen, where he graduated M.B. with honours in 1897, he was awarded the Fife Jamieson gold medal in anatomy, the Shepherd gold medal in surgery, and the Struthers gold medal in anatomy. In 1900 he settled in practice in Belgravia and the following year he took the degree of M.D. with commendation.

During his twenty five years in general practice he lived a comfortable and, to outward appearances, contented existence. But he was not really happy in ork. Even as a student he had been of an inquiring and as he did not find an outlet for this in general ce he turned his attention to laboratory research. Lister Institute was nearby and the head of the riological department in those days was Professor er Sir John—Ledingham who had been a fellow ent at the University of Aberdeen It was presum- through Ledingham that Lumsden obtained the oduction to Sir Charles Martin, director of the itute, which started him on a research career At t he gave only a part of his time to his investigations would look in at the Lister when going the round of patients, make an experiment, and then dash off ain to his practice Gradually he became more and ore absorbed in his laboratory work until he decided give up his practice and devote himself entirely to search, and in 1925 he became an honorary assistant the pathology department of the institute At first e was interested in the existence of supplementary espiratory centres, but soon cancer occupied all his attention, and in 1928 he moved to the London Hospital, where two years later he was appointed director of cancer research

With the outbreak of war and the dispersal of the London Hospital and its medical school over Essex and the adjoining parts of Middlesex and Hertfordshire, Lumsden was moved to Chase Farm Hospital at Enfield Here he was given laboratory space and the opportunity of putting the finishing touches to his researches with a view to writing up his work on anti-cancer sera. Towards the end of the war, this work accomplished, he retired from the London Hospital and went to live in Hertfordshire.

A former colleague writes "Like others before him, Lumsden was imbued with the idea of making an anti-cancer serum, and to this end he devoted himself with a fervour which was almost religious. He imagined at it might be possible one day to treat malignant dis- se by means of antisera it was as simple as that, saw his problem clearly in black and white and he t himself to solve it with the optimism born o nthusiasm What did he achieve in all the years he evoted to cancer research? It is sad to think that so nuch thought and skilful work should have left so nsubstantial a record, though one hastens to say that this was hardly his fault. He had his critics it is true, but it would be the greatest mistake lightly to dismiss Lumsden and his work. He was single-minded in his enthusiasm for his research and he believed so strongly in himself and his mission that he was prepared in middle age to abandon the security and affluence of a well-established practice for a research post without any assured future Had he been better trained in the scientific method and had he been a little more amenable to guidance, he might well have left a better record of achievement

"Lumsden was a difficult man to know At work he was on the friendliest terms with his colleagues, but none was allowed to intrude into his private life It was known that he lived in Chelsea, but where exactly was not recorded. One of his recreations was drawing, for a time he was a member of a life class in Chelsea and his work showed that he was not without talent. He enjoyed orchestral music, particularly Wagner But it was at work in his laboratory that he undoubtedly found his greatest happiness"

In our obituary of Mr T G Stevens (Nov 21) we stated incorrectly that his wife survived him Mrs Stevens died on April 2 of this year

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Appointments

BODMAN R I M.B. Brist D A anaesthetist (consultant), St. Peter's, St Paul's, and St. Philip's Hospitals, London.

BURKE JOYCE M D Lond M R C.P D OBST asst. medical registrar The Hospital for Sick Children, Great Ormond Street, London

MARTIN L V M.B. Lond D A. consultant anaesthetist, North Gloucestershire clinical area.

ROSS, DAVID M.B. Glasg, F R.F P.S. physician-superintendent (consultant) Stratheden Hospital, Cupar Fife, and Strathore Mental Deficiency Institution

WAGNER, JOAN M.B. Witwatersrand, M.R.C.P asst. medical registrar, The Hospital for Sick Children, Great Ormond Street,

Notes and News

A GREAT PHYSIOLOGIST

Torsten Thunberg was almost 80 when he died on Dec 1952, after a short illness initiated by a fractured femu was actively engaged in research until the very end his last paper—a review of citric-acid metabolism—was lished in *Physiological Reviews* a month after his de Thunberg will always be remembered for his work on biolo oxidations, which he pictured as proceeding by the enzym activation and subsequent transference of 2 hydrogen from the molecule undergoing oxidation to some hydrogen acceptor which might be another cellular compo or oxygen itself, or, for experimental purposes, methy blue. This conception enabled biochemists to visualis explore the controlled oxidations which character cells far better than the idea of an "active" or acti oxygen could ever have done, and was the inspiration of of the great work on cellular oxidations carried out in bridge between the two world wars. Thunberg was o those men whose genius overcame physical limitations department was very small and so limited in numbers th was never able to build up a great school Neverthe lived to see the creation of one of his heart's desires—the physiological institute at Lund, which is devoted very to research

Mural tablets are dull things, and even bricks and offer scanty satisfaction to the creative mind Workers a new institute, therefore, decided to dedicate a supplem the 30th volume of *Acta Physiologica Scandinavica* to t great predecessor, and the book contains their tributes memory and inspiration in the shape of nineteen or papers on various aspects of physiology

APPROVED NAMES FOR DRUGS

THE British Pharmacopœia Commission has issu following new supplementary list of approved names

Approved name	*Other names*
Amodiaquine	7-Chloro-4-(3-diethylaminom 4 hydroxyanilino) quinoline Camoquin
Azovan Blue	Tetrasodium salt of 4 4′ bis[illegible] amino-8 hydroxy 2 4-di[illegible] naphthylazo] 3 3′ bitolyl Evans Blue.
Carbomycin	An antibiotic produced by [illegible] of *Streptomyces halstedii* Magnamycin.
Laudexium Methylsulphate	Decamethylene-1 10 bis 1-(3 4 dimethoxybenzyl)-1 2,3,4-tetra hydro-6 7 dimethoxy-2 isoquinolinium methylsulpha Laudolissin.
Meclozine	1-p-Chlorobenzhydryl 4-m-me benzylpiperazine. Ancolan is the dihydrochlorid

RESEARCH ON DELINQUENCY

As a rule an aura of youth and inexperience surrou second annual report, but this does not apply to the report[1] of the Institute for the Study and Treatm Delinquency which was incorporated last year This of course, is identical with the Institute for the Treatment of Delinquency which has been in action was founded by the late Dr E T Jensen in 193 Portman Clinic which he also founded now operate National Health Service under the ægis of the Pad Hospital Among the research projects sponsored institute are an inquiry into the part played by low in in the causation of delinquency, a statistical stud delinquent boys aged 7–17 seen at the Portman 1952–53, and a study of the effect of œstrogens offenders A joint committee of the institute and th League for Penal Reform has been set up to ma investigation of cases of cruelty to children, Commissioners have agreed to allow those senten the past year for offences involving cruelty to chi examined psychiatrically, and a concurrent stu made of the social, economic, and cultural ba the families in which the cruelty occurred

The institute conducts extension lecture co diploma in social studies, and for the new dipl logy, of the University of London, and also a and courses on delinquent and criminal behaviour for psychiatrists. It offers study courses for magistrates assists with the Home Office courses for probation officers in training and arranges lectures for prison officers A summer school is to be held next year at Oxford from Sept 18 to 25 on the Changing Attitude of Society to Criminal Responsibility The Paddington Hospital Group Management Committee have made two grants, each of £50, to the Portman Clinic, for the purchase of medical books. These are being added to the Jensen memorial library, and books have also been bought with a grant made by the trustees of Dr Jensen Among the publications of the institute are the *British Journal of Delinquency*, now in its fourth year, and a range of pamphlets on psychiatric and criminological subjects

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[1] Annual Report 1952–53 Institute for the St ment of Delinquency, 8, Bourdon Street, Davies W 1

CARDS FOR CAUSES

The British Epilepsy Association have just notified us that this year they too, are selling Christmas cards and Christmas seals. The cards, which are sold at 5*s* 6*d* a dozen postage paid, carry a design by Hero of Father Christmas skating and at the same time juggling in a reckless manner with five stars. The seals bearing the candle design which is the emblem of the association, are sold at 1*s* for a sheet of 48 Both may be had from the association, 136, George Street, London, W 1

JAMES BRIDIE S DRAWINGS

The late Dr O H. Mavor (James Bridie) saw an exuberant and ludicrous world, and drew what he saw with genial gusto In his drawings of university personalities at present on exhibition in the print room of the Department of Fine Arts at Glasgow University he pulls the legs of the great men of yesterday and today mischievously and without malice The great Sir William Macewen quizzes a hapless medical superintendent remembering his name but failing exactly to recollect his face Sir Robert Muir in his laboratory disreputably dressed, flatly rejects the offer of a new coat from his immaculate assistant the future Professor Shaw Dunn. One surgeon is shown introducing martial law into his theatre A second receives from an urbane medical colleague an unwelcome lesson in medical deportment There are grotesque but wholly successful caricatures of the formidable Sir Donald MacAlister of Murdoch Cameron in a bathing suit, of a prognathous and discursive E P Cathcart and one can even see Graham Kerr dividing by binary fission.

FILMS AT LONDON MEDICAL EXHIBITION

More films but fewer new films than in previous years were shown at the London Medical Exhibition last month. A very good French film on *The Cyto-Diagnosis of Uterine Cancer* (25 minutes; sound colour) with an English commentary shows the collection of biopsy specimens and the staining and appearance of the sections by cinemicrography The two parts of the film are detailed and each part appears to have been intended for a different audience though the whole film will be appreciated by both clinicians and pathologists *Gastrectomy with Jejunal Replacement* (20 minutes sound colour) demonstrates the operation which was the subject of a Hunterian lecture by Mr F A. Henley earlier this year The procedure is clearly shown and readily understandable by gastric surgeons; but those less familiar with the Billroth operations will gain little from the film. On the other hand, no previous knowledge of the subject is necessary to understand and enjoy *Marrow Puncture* (33 minutes sound, colour) The technique of sternal puncture is shown both on a patient and on anatomical models and other sites suitable for marrow puncture are demonstrated The film ends with a farcical section in which the advice given in the film is ignored *Nalorphine* (10 minutes sound colour) deals with the response in dogs deeply narcotised with morphine and other opiates to the intravenous injection of the new drug A large clock is started as the injection is given and the dogs recover fully quite suddenly some ten to twenty seconds later *Pentothal Its Use in Intravenous Anaesthesia* (45 minutes sound colour) is disappointing. The film is in the form of a chat between an anæsthetist and a student mostly in the surgeon s room whilst they are awaiting the arrival of a patient for operation Periodically the anæsthetist s words are illustrated by scenes of an anæsthetist at work in the anæsthetic room and theatre, and at one stage the student is taken to another room to see a film of thiopentone being used. *Reduction of Surgical Hæmorrhage by Controlled Hypotension* (42 minutes; sound, colour) is a detailed exposition of the use of hexamethonium compounds during anæsthesia by means of demonstrations in the operating theatre animated diagrams, and puppets. A new American film *The Antibiotics and Terramycin* (22 minutes; sound, colour) deals rather superficially with the history of antibiotics and the use of terramycin The British *Venepuncture* (14 minutes sound colour) is designed for general practitioners and gives valuable hints on minimising trauma

MEDICAL SCHOOLS OF THE WORLD

THE World Health Organisation has published the first *World Directory of Medical Schools* (H.M. Stationery Office. 25*s*) which lists more than 500 medical teaching institutions distributed over 84 countries. With so much ground to cover the editors have wisely restricted the information they offer about each school to such salient facts as number of students and staff duration of studies, and fees. Even so there are not unexpectedly a number of blanks in their informative pages.

University of Oxford

On Nov 21 the degree of D M was conferred on P B S. Fowler

University of London

At a recent examination for the academic postgraduate diploma in psychological medicine G F Vaughan and Lorna Wheelan were successful.

Queen s University, Belfast

Dr R A. Womersley has been appointed to a lectureship in medicine

Royal College of Obstetricians and Gynæcologists

At a recent examination for the D OBST the following were successful:

G. A C Abraham, R. D Allen J P Alvey A. G Amias, J A. D Anderson J R. Angwin J H Armstrong Robert Bain, D A. Baird Doreen S. Ball, G V Balmforth, J A. C. Bamford, A A Bapty A P Barclay, N H Barley H C Barr A G. Beatty H R. C Benny W G Benson J S. Berkeley, Margaret S. Beverland J R. Billinghurst, Dorothy G Blackett-Ord, R. C. Bloomfield D G Bluett, Audrey A. Bontwood, Iona M Brereton, R W Brotherwood, B J Brown, C. T Brown G L Brown, J D Bruce, C. V Bullen A K. Burt, Seonaid C. Cameron Patricia E Campbell, R. W Campbell, Reginald Carr Sumathi R. Chandy Sin Gian Chua, B W Cole, P F A. Crawshaw Barbara M. St. J Coventry, H J E Cox, G E Crawford P M Crawford, Flora M Dale G M Davidson, L F Digby Josephine Dolan, K O. Easton, Barbara C. Edwards B D Ellis, Doreen A Ellis, Lionel Elton, H. A Evans Margaret O Fairman, D C Faull L. C Fernandez, F L. Firth, J A. Fleming Marjorie H. E. Flowerday D S. Foster I H Gardner W A. Gentle, W J Glover Mervyn Goodman, Leonora H Goulty C W. Grant, Monica C Grant, Cary C Griffiths, Joan M. Halliwell, Elinor C. Hamlin J L. Hanington, Maureen E Hardeman, J G Hayes, Margaret A. Hayes, John Hennigan J R. Hewett, Michael Hewett J D Jackson, R. J Jameson, Andrew Jervis, D D Johnstone G. M. Johnstone, Zohra Begum Kazi, T W Kidd, F F Kinnaird, W A. Kirkpatrick T P Kissack, R. L. Kleinman, Mukulika Konar Yu Shing Lam A. N Horwitz, Sheila M Lane, A S Liddell Ruth Lister Mary I Lloyd, Anne E. T Lodge W H McBay, T D McCarthy Jessie Macdonald, Morag S Macdonald, John MacIntosh M J McKenna, Alexander Mackinnon, J H. Marks, Helen F Martin, J B. H Martin, P L Martin, D G May, Prabha Mehra A. H Mendoza, B R. Middleton, N A. Miles R. H. D Miles, A P Millar A P Miller D D Moir Marjorie Monk, J L. Montagnon, R. D Morbey D F Morley J D Morris, E. A Murray Joan M. Nabarro Shirley E. Nathan R. W A Nel, P A. Normandale, R. O Norton, K. C. Nyman, Irene M F Ondatje, Heather M Panton, E. R. Parry Mary C W Paterson, D C. Pattison Peter Pan, Barbara M. Philpott, A. C. C. Pinion, G H. G Poole Gertrude M Pullan, T A I Rees, J G Rider, K. J Roberts Charles Rooney J J O'C. Rorke, A D Rose Leslie Rose, D P Rough, Prokash Chandra Roy, F C. Rutter P E. H. Rutter R. G Seager-Thomas, Noel P Shannon, James Sharp, Mary E. T Sheridan H A. D Shirlaw, J Ll Skinner A. I Smith, D P O Smith Lindsay Smith, R. C. Smith, A. G Stephens, Monnica C. Stewart A. M. Stoble G F. Stone H. L Symon, G W. Taylor Mary T Taylor J C. Turner Barbara V Tyman Lilian S. Underhill, T W West, I J Waite, Mary J Watson, J N Wattie, H. B G Webb A. L. Wells, W G Wenley Constance M Wilkinson F C Wilkinson, Ronald Williams, E. A. Wilson, Janet W Worling Margaret E. Wort, Victor Zuck.

Royal Medico-Psychological Association

At recent examinations for the D.P M. the following were successful:

J D C. Currie R. S. Ferguson, T E Hall I. E. J McLauchlan M. J Raymond, A. Smellie, Elizabeth Shoenberg

Harveian Society of London

The subject for the Buckston Browne prize (£100) for 1954 is to be Medical Problems of the Overweight Patient Essays should reach the hon. secretaries of the society, 11 Chandos Street, W 1 by Dec 1 1954

Royal Microscopical Society

At a meeting of this society on Wednesday Dec 16 at 5.30 P.M., at Tavistock House South, Tavistock Square London, W C 1, Mr R W G Wyckoff will speak on the Electron Microscopy of Viruses.

School Dentists

Speaking at Wakefield on Nov 27 Miss Florence Horsbrugh, Minister of Education, said that there were now the equivalent of 928 full-time dentists in the school dental service This was the highest figure so far recorded

Medical Association for the Prevention of War

The London branch of this association is holding a forum at 8 P M on Wednesday, Dec 9, at 45, Russell Square, W C 1, on the theme of Racial Discrimination, when Prof L S Penrose, F R S, will discuss the scientific basis of racial theories

Journées Médicales de France et de l'Union Française

Prof C Lian will preside over the journées which are to be held in Paris from April 21 to 24 Medicine and the Improvement of Life has been chosen as the general topic for the meeting Further particulars may be had from the secretariat, 12, rue Pierre Geofroix, Colombes (Seine)

Anglo-French Exchange Bursaries

Applications are now invited for bursaries which will be awarded in 1954 to young British doctors under the exchange scheme arranged by the French Embassy in London between the Institut National d'Hygiène in Paris and the Ciba Foundation in London

The grants (60,000 francs a month) will be awarded for two to four months to doctors who wish to obtain clinical experience or carry out medical research in France Application forms may be had from Dr G E W Wolstenholme director of the Ciba Foundation 41 Portland Place, London, W 1 The closing date for applications is Feb 22

Medical Artists' Association

Work to be submitted for the examination for the membership of this association should reach Miss Audrey Arnott, The Rotunda, Radcliffe Infirmary, Oxford, by Jan. 31 Application forms may be had from the hon. secretary, Miss Margaret McLarty, at the same address

International Organisation against Trachoma

The next meeting of this body will take place at Montre on Sept 11, 1954, under the chairmanship of Mr A. MacCallan. Offers of communications should be sent to secretary general of the XVII International Congress Ophthalmology, 100, 1st Avenue Buildings, Rochester, Mi U S A

British Association of Urological Surgeons

The annual meeting of this association will be held next year from June 24 to 26 in Dublin, under the presidency Mr Terence Millin The main subject chosen for discus is Irradiation Therapy in Urology Dr G W Blomfield wi be the opening speaker, and Mr E W Riches, Mr D Poole Wilson, Mr J D Fergusson, Mr R Cox, and M D M Wallace will also take part

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The *Proceedings of the First International Congress on Medi Records*, which was held in London in September, 1952, have now been published Copies may be had from the hon. secretary of the Association of Medical Records Officers, Christie Hospital, Wilmslow Road, Manchester (26s plus postage)

Diary of the Week

DEC 6 TO 12

Monday, 7th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W 12
4 P M Prof. A. Haddow Recent Trends in Experimental Pathology of Cancer

UNIVERSITY COLLEGE, Gower Street, W C 1
4 45 P.M Mr H Gutfreund, PH D Molecular Forces in Protein Solutions (First of two lectures.)

ROYAL EYE HOSPITAL, St George's Circus, S E 1
5 15 P M Dr T H Whittington The Refraction Case—Six Factors Producing Good Sight.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, W 1
5 P.M Sir Henry Dale, O M, F R.S. Changes and Prospects in Medicinal Treatment. (First of three Harben lectures)

HUNTERIAN SOCIETY
7 30 P M (Talbot Restaurant 64 London Wall E C 2) Dr J Aldren Turner Mr H Osmond Clarke A Pain in the Neck

Tuesday, 8th

ROYAL COLLEGE OF PHYSICIANS, Pall Mall East S W 1
5 P.M Dr Maurice Davidson Medicine in Oxford—A Historical Romance. (First of two FitzPatrick lectures)

UNIVERSITY OF LONDON
5 30 P.M (University College) Prof Otto Koehler (Freiburg) Thinking Without Words

ROYAL EYE HOSPITAL
5 P M Prof. Arnold Sorsby Nature of Congenital Anomalies.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE
5 P.M Sir Henry Dale Changes and Prospects in Medicinal Treatment. (Second of three Harben lectures)

INSTITUTE OF DERMATOLOGY St John's Hospital, Lisle Street W C 2
5 30 P.M. Dr P D Samman Reticulosis.

WEST END HOSPITAL FOR NERVOUS DISEASES 40, Marylebone Lane W 1
5 30 P M Mr I R McCaul Investigation of Cerebral Tumour

CHELSEA CLINICAL SOCIETY
7 30 P.M (South Kensington Hotel, 41 Queen's Gate Terrace S W 7) Mr Dickson Wright Dictators and their Doctors

MANCHESTER MEDICAL SOCIETY
3 P.M (Medical School University of Manchester) *Section of Surgery* Prof. C G Rob Arterial Grafting

Wednesday, 9th

ROYAL COLLEGE OF SURGEONS Lincoln's Inn Fields W C 2
4 P M Sir Reginald Watson Jones Fracture Treatment in the Next Half-century (Bradshaw lecture)

POSTGRADUATE MEDICAL SCHOOL OF LONDON
3 P.M Prof G M. Bull Tests of Renal Function (First of three lectures)

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE
5 P M Sir Henry Dale Changes and Prospects in Medicinal Treatment. (Last of three Harben lectures)

INSTITUTE OF DERMATOLOGY
5 30 P.M Dr H Haber Reticulosis

INSTITUTE OF NEUROLOGY National Hospital, Queen Square W C 1
5 P.M Dr H Hécaen (Paris) Balint's Syndrome and its Minor Forms.

INSTITUTE OF PSYCHIATRY Maudsley Hospital Denmark Hill S E 5
[illegible] Dr Eliot Slater The McNaughten Rules and Modern Concepts of Responsibility

INSTITUTE OF UROLOGY, 10 Henrietta Street, W C 2
5 P.M Mr J G Sandrey Urological Emergencies in Gener Practice

BIRMINGHAM MEDICAL INSTITUTE, 154, Great Charles Stre Birmingham, 3
8 P.M *Section of Psychiatry* Dr R. A. Sandison Place of Ar Therapy in Treatment of Mental Illness.

MANCHESTER MEDICAL SOCIETY
4 30 P.M (Medical School, University of Manchester) *Section Pathology* Dr W C Cockburn Field Investigations Whooping-cough Vaccines.

Thursday, 10th

ROYAL COLLEGE OF PHYSICIANS
5 P.M Dr Davidson Medicine in Oxford—a Histor Romance (Second of two FitzPatrick lectures.)

ROYAL COLLEGE OF SURGEONS
5 P.M Mr St. J D Buxton Arthroplasty (Robert J lecture)

ROYAL SOCIETY, Burlington House, Piccadilly, W 1
4 30 P M Sir Francis Walshe, F R.S Contribution of C Observation to Cerebral Physiology (Ferrier lectu

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, 26, land Place, W 1
7 30 P.M. Dr Henry Foy Influence of Intestinal Fl Synthesis of Hæmopoietic Factors in Megalob Anæmia of Africans

POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 30 P M Professor Bull Tests of Renal Function. (Second of three lectures.)

ROYAL ARMY MEDICAL COLLEGE, Millbank S W 1
5 P.M Dr G S Wilson Work of Public Health Laborator Service

INSTITUTE OF CARDIOLOGY, National Heart Hospital, Westmorela Street W 1
9 30 A.M. Dr Maurice Sokolow (California) Quinidin

INSTITUTE OF DERMATOLOGY
5 30 P.M Dr R W Riddell Superficial Fungous Infection Skin

ALFRED ADLER MEDICAL SOCIETY
8 P M (11 Chandos Street W 1) Dr L P E Laurent Psychosomatic Effects of Obesity

Friday, 11th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 30 P.M Professor Bull Tests of Renal Function (Last three lectures.)

INSTITUTE OF DERMATOLOGY
5 30 P.M Dr Samman Reticulosis

OSLER CLUB OF LONDON
7 15 P.M (11 Chandos Street W 1) Dr Leonard Colebr F R.S Emile Roux (1853–1933)

Saturday, 12th

BIOCHEMICAL SOCIETY
11 A.M (London Hospital Medical College, Turner Street, E.1. Scientific papers

SOUTH EAST METROPOLITAN REGIONAL TUBERCULOSIS SOCIETY
10 30 A.M (King's College Hospital Medical School Denma Hill S E 5) Dr Clifford Hoyle Dr John Dawson, I Gordon Mather Sarcoidosis

Births, Marriages, and Deaths

BIRTHS

GRIBBLE.—On Nov 28 at the London Hospital, to Mary (née Watkins) wife of Michael Gribble, M.A., B.M—a son (Julian de Gruchy)

THE UNIVERSITY AND SURGERY*

M F A Woodruff
M.D., M.S. Melb F R C S
ROFESSOR OF SURGERY IN THE UNIVERSITY OF OTAGO
NEW ZEALAND

r is salutary for every university teacher to consider own particular discipline in relation to the purpose of university as a whole But what is the purpose of a versity ? I propose to examine three fundamentally erent answers to this question and to discuss their nificance for a teacher of surgery

he first, which Sir Walter Moberly (1949) calls the tian–Hellenic answer, is embodied in Newman's *e of a University* (1852) It affirms that the main ective of a university is intellectual culture True versity education thus avoids narrow specialism, on one hand, and superficiality, on the other, it

> ves a man a clear conscious view of his own opinions l judgements, a truth in developing them, an eloquence in ressing them, and a force in urging them It teaches to see things as they are to go right to the point, to ntangle a skein of thought, to detect what is sophistical l to discard what is irrelevant It prepares him to fill post with credit, and to master any subject with facility '

he second, or in Moberly's terminology the *liberal* wer is that the prime object of a university is the suit of new knowledge for its own sake irrespective its possible applications Communication of know ge, especially at undergraduate level is of secondary portance

The third, or *technological and democratic* answer is dominantly utilitarian It affirms that the function a university is to Serve the state by providing the perts and the ideas necessary to maintain material gress. Education must be strictly vocational, and the ue of research depends on whether or not it provides ults of practical importance. Learning for learning's ke is an idol to be demolished and, as Moberly puts it, the hero, or archetypal figure is the man who makes o blades of grass grow where one grew before This cept reflects the enormous development of applied ence and gains much of its strength from the fact that is just in this field that the universities are most closely touch with what Ortega denotes by culture "the al system of ideas of a period" (Ortega y Gasset 1946)

It is clear that these three concepts, if pushed to tremes, are mutually incompatible I believe never less that each contains elements of truth and that a thesis can and must be made I submit in short, at intellectual culture, vocational training and research form part of the complex function of a university

Intellectual Culture

Intellectual culture is certainly of fundamental portance For as Newman observes a cultivated ellect, because it is good in itself brings with it a wer and a grace to every work and occupation which it dertakes.' How may it be achieved ? It is not, in elf, a branch of knowledge but rather a healthy state of nd which can be developed only by study in some propriate field. As Newman remarks

> 'In saying that law or medicine is not the end of a versity course I do not mean to imply that the university es not teach law or medicine. What indeed can it teach all, if it does not teach something particular ?

This at once raises the question of what subjects and ares of study fall within the province of a university The vice-chancellor of Queen's University Dr Eric hby (1946) has suggested the following answer

> 'If the subject lends itself to disinterested thinking ; if generalization can be extracted from it ; if it can be advanced by research if in brief it breeds ideas in mind, then the subject is appropriate for a university If on the other hand the subject borrows all its principles from an older study (as journalism does from literature or salesmanship from psychology or massage from anatomy and physiology) and does not lend itself to generalization, then the subject is not a proper one for a university Let it be taught somewhere by all means but it is a technique not an exercise for maintaining intellectual health and the place for a technique is a Technical College

This answer is good so far as it goes, but it rather suggests that we may divide all conceivable subjects of study into two clearly defined categories—those which are technical and those which, for want of a better word, may be called cultural This is a dangerous fallacy and one to which academic people are liable it might well be called in Francis Bacon's terminology an Idol of the Quadrangle A more accurate view is expressed by Professor Montrose (1952), also from Queen's University who distinguishes three levels of education which he calls technical specialist, and general :

> *Technical education* may be briefly described as indoctrination. It does not consist in the mere imparting of factual information for theories may be taught and skills practised, while ability to apply knowledge to particular situations may also be required But the understanding is limited since acceptance of existing doctrine is assumed. The student submits to learning he does not master it by developing a real understanding, which comes from a creative and critical approach.
>
> *Specialist education* embraces technical education but proceeds to a higher level. It introduces the critical and creative approach by making the student aware of the problem character of the discipline and of the strength and fallibility of human solutions and problems, and also by inspiring him with the ideal of seeking for better solutions.
>
> *General education* embraces specialist study but takes it to the higher level appropriate to universities by making the specialist aware of the broad topics and general methods of other disciplines Without specialist study there is no penetration to the heart of the subject no travelling to its periphery where its relation to other subjects may be appreciated without general education the process required by the specialist approach itself is halted There are broad problems and *general methods common to many disciplines*, and progress in each is best assured by awareness that solutions of particular problems in each may be suggested or even elaborated in some other discipline

Professor Montrose's thesis does not differ essentially from that presented two years ago by Sir Harold Himsworth in a stimulating address on the University and Medicine in which he stated that the real difference between education and technical training is one of aim and purpose Himsworth made the further very important point that all education has its basis in technology

> Custom, he said has habituated us to the euphemism that learning the techniques of reading writing and mathematics, and acquiring a knowledge of foreign languages, are educative processes. But education in the higher sense the development of power to form judgments only becomes possible after such techniques have been acquired It can therefore be conceded at once that a modicum of detailed and technical knowledge is an indispensable foundation for higher education, be this classical or scientific. But this modicum must be such as to form the basis for the development of a representative selection of intellectual skills (Himsworth 1951)

Admittedly with some subjects it is almost impossible to get above the technical level ; in many others however the level reached depends rather on the teacher and the student than on the subject itself It has been abundantly proved that a study of the Classics can be a potent means of intellectual cultivation but that is not the only way The study of history philosophy modern languages, and literature, and (dare I add ?) mathematics physics, chemistry, and biology may be no less effective. Moreover it is well to remember that the study of any subject, including the so-called humanities, if wrongly conducted, can be a stultifying experience Byron's *Thoughts Suggested by a College Examination* are a pertinent reminder

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* Inaugural lecture in the chair of surgery University of Otago medical school New Zealand, 1953

> " Happy the youth in Euclid's axioms tried
> Though little versed in any art beside ,
> Who, scarcely skill'd an English line to pen,
> Scans Attic metres with a critic's ken.
>
> Though marvelling at the name of Magna Carta,
> Yet well he recollects the laws of Sparta ,
> Can tell what edicts sage Lycurgus made,
> While Blackstone's on the shelf neglected laid ,
> Of Grecian dramas vaunts the deathless fame,
> Of Avon's bard remembering scarce the name
>
> Such is the youth, whose scientific pate
> Class-honours, medals, fellowships await."

Vocational Training

Today, with the almost complete disappearance of the leisured class, the demand for vocational training is greater than ever before In many vocations the essential qualification is the ability to perform certain clearly defined tasks and to react correctly to stock situations ; for these training at technical level is sufficient There are other vocations, however, exemplified by the so-called learned professions, for which purely technical training is hopelessly inadequate These demand, in addition to specialised knowledge and special skills, educated minds capable of dealing with new and complex situations It seems self-evident that recruits for these professions need both a university education and a period of professional apprenticeship , the real point at issue is the extent to which university studies should relate to specific professional requirements My own view is that professional training can be of great vocational value and is by no means incompatible with Newman's concept of the university's function Moreover, if professional training and university education are divorced, the former will almost inevitably be conducted at a purely technical level, and the latter is likely to be superficial or even perfunctory I therefore hold that the practice, which has been followed since the Middle Ages and which Newman himself accepted as proper, of the universities assuming a large measure of responsibility for training recruits for some at least of the professions is sound, and indeed essential, provided always that the objectives we have been discussing are kept clearly in view If this plan is adhered to a period of apprenticeship is still necessary, but it can be effectively integrated with the early training , and in some instances, as in Medicine, it *may begin before graduation*

The objection may be raised that the universities' hands are tied because, to an ever-increasing extent, entry into the professions is being controlled by bodies such as the Law Society and the General Medical Council, which prescribe courses of training and either conduct, or in large measure control, qualifying examinations.

It is certainly conceivable that this might give rise to difficulty , in fact, however, it does not appear to have *done so* Certainly, *so far as the profession of medicine* is concerned—and this is the only profession for which I can speak—the General Medical Council in Britain, and corresponding bodies in the Dominions, have done an enormous amount to raise professional standards without exerting any harmful influence on the universities

Research

The search for truth is complementary to the other *functions of a university Not only is the cultivated* intellect of vital importance in this search , the pursuit of any scientific discipline is a potent means of promoting intellectual growth and of developing that imaginative insight which, as Whitehead (1932) has used, is the hallmark of the educated man

The search must be free and unfettered
siderations of expediency This claim is often
on the ground that a discovery which does n
to have any immediate application often prove
be of great practical importance, but this is be
question. I believe, as anyone undertaking fur
research must believe, as an article of faith, th
worth pursuing for its own sake. It is nat
indeed salutary, to have periods of doubt about
it is comforting to find that scientists of the
Sir Macfarlane Burnet have experienced suc
(Burnet 1948), but we must overcome them.

At the same time we must avoid the opposit
of despising research of an ad-hoc kind. S
application is certainly not essential, but to
consider the impact of discoveries on the profes
in industry or, worse still, to avoid deliberately
which seem likely to have a short-term appl
surely academic affectation of a most objection
Happy indeed is the man whose work com
possibility of fundamental discovery with the s
immediate problems, for he easily avoids bo
errors.

The Place of Surgery in the Universit

We are now in a position to consider the
surgery in the university It will be conve
arrange the discussion under three main h
undergraduate education, postgraduate traini
research.

UNDERGRADUATE EDUCATION

The medical student begins by studying t
sciences of physics, chemistry, and biology ; he t
on to study the structure and function of the
body After three years, while still an underg
he becomes an apprentice, and is brought into
with men, women, and children ill in mind or b
begins to learn something of the value, and th
tions, of the scientific method applied to the
disease , and at the same time he is introduce
human and social problems occasioned by birth,
old age, disease, and death.

It is hard to imagine a more enriching experie
field of study better calculated to bridge the wide
between the humanities and the sciences , Why
the level of *general education attained* by the
student so disappointingly low ? I believe t
explanation lies not in the nature of the subjects
nor in the calibre of the students, but in our t

In the first place, we have been too much sy
demands from various sections of the profession t
this or that because it will be important in practic
object should not be to produce general practi
or surgeons, or pathologists, or research-worke
graduates who are totipotent, being capable of di
ating during the postgraduate phase of their app
ship in various ways according to their ind
abilities, inclinations, and opportunities.

Secondly, we teach too many facts. There
many subjects that few if any are studied
cramming is almost inevitable, and the student h
time to think for himself

Thirdly, insufficient effort is made to help s
with the difficult intellectual and psychological
ments necessitated by the transition from prelin
clinical work.

The position cannot be improved by introducin
so-called cultural subjects The right approach
prune, and to set each subject in proper perspect
asking ourselves how much a student can reaso
expected to learn about it, what contribution it can
towards general education, and how it should be t

Let us try to answer these questions as r
surgery

How much Surgery should a Student be Expected to Learn?

In my own university it was customary to publish in the calendar a syllabus for each subject in which degree examinations were held. Under *Surgery* one found the alarming pronouncement that *the syllabus includes the whole subject.* Fortunately our teachers were too wise to treat this seriously, or our state would indeed have been parlous. In contrast it is sometimes suggested that since only a small proportion of students are going to be surgeons, and then only after years of postgraduate training, there is no need to teach surgery at all.

Most surgeons, and most teachers, would reject both these extremes: the first because the surest way of teaching too little is to try to teach too much, the second because, as I have already tried to show, it is based on a misconception of the nature and purpose of medical education. There is, however, much difference of opinion regarding the precise direction we should take.

My own view is that when a student sits for his qualifying examination he should have learnt to take an accurate history and to conduct a proper physical examination, and should be able to diagnose common surgical disorders, especially those requiring prompt treatment. In cases where he is unable to make a precise diagnosis he should know when and where to seek expert advice. Finally, he should be familiar with the principles underlying the treatment of patients before, during, and after operation, and should have a general idea of the scope and the limitations of present-day surgery.

Even this modest goal is not always reached. But if the teaching of medicine and surgery are properly coordinated, and if both are based on a firm foundation of anatomy, physiology, and pathology, it should be well within the reach of every student who does his work in the wards and the outpatient department conscientiously.

What Contribution can the Study of Surgery make towards a Student's General Education?

In the first place, it is not difficult to relate the study of surgery to that of other subjects. The most obvious links are with other clinical subjects and with the biological sciences, but there are many more. Contact with patients inevitably introduces psychological problems, and experience of suffering, even if vicarious, raises issues of profound metaphysical and theological import. These issues form the subject of an immense amount of literature, in which the student may browse at will: his main difficulty is to know where to begin. And if yet more links are required, one may consider the history of surgery, or the effect of surgical progress on the history of mankind.

Secondly, surgery provides excellent opportunities for training students to make accurate observations. And it is, I believe, all to the good that in many cases observations of crucial importance have to be made with the unaided senses.

Thirdly, the student learns to draw reasonable inferences from his observations. His capacity for logical thinking grows, and he develops a capacity for making sound intuitive judgments when logic can carry him no further. It is important for him to learn to distinguish between these processes, and to determine by introspection how he has reached a given conclusion. This naturally raises questions of an epistemological character, and the student who wants to pursue them can be introduced to Locke, Hume, Kant, Russell, Whitehead, and the rest.

Finally, the student learns to make up his mind. Of course the ultimate decision about what treatment to advise rests with the surgeon in charge of the case, but it is, I think, essential for the student to decide what he would do if the responsibility were his. It is far better for him to make mistakes than to remain for ever a prey to indecision. In surgery, more often than in medicine, important decisions have to be made quickly, and it is perhaps this fact, more than anything else, which gives to the study of surgery its distinctive character.

How should the Teaching of Surgery at Undergraduate Level be Organised?

Lectures, lecture demonstrations, and bedside instruction are all of value, but I am wholeheartedly in agreement with Mr David Patey when he says that the pivot on which the whole British system of clinical instruction turns is association of the undergraduate with the work of the various clinical units in an active responsible capacity. This requires a high ratio of patients to students and a curriculum which leaves plenty of free time for ward work (Patey 1952).

This system was developed in the days of honorary hospital staffs. Today almost everyone is paid, but it is still possible, and in my view essential, for much clinical teaching and supervision to remain the responsibility of men engaged in the hurly-burly of private consultant practice. To keep a proper balance, however, and to achieve continuity between preclinical and clinical work, this responsibility should, I believe, be shared with men who are full-time members of the staff of a university. Such men must be competent surgeons, and they must therefore be actively engaged in surgical work. In addition, however, they must be interested in education in the widest sense of the word.

My distinguished predecessor has suggested that it is nowadays impossible to be a professor of surgery because the field is so vast that no-one can compass it: he therefore favours the title 'director of clinical studies.' Mr Patey, too, appears to be of the same opinion. With great respect I disagree, for what is needed is not merely someone to coördinate clinical teaching but also someone to bridge the gap between hospital and university, someone able to speak in the university on behalf of the profession and to foster in the hospital the ideals of the university. Exhaustive knowledge is fortunately not necessary. If it were, there would be no professors not only of surgery but also of mathematics, physics, history, philosophy, and every other subject worthy of a university.

POSTGRADUATE TRAINING

The main responsibility for maintaining professional standards in surgery rests with the Royal Colleges. It is therefore in my view both right and inevitable—though it is sometimes deplored in university circles—that the colleges should to a large extent determine the pattern of postgraduate training, and should conduct examinations. It is also right and inevitable that the medical graduate who wants to become a surgeon should spend some years in hospital posts, working first under close supervision and later enjoying a measure of responsibility commensurate with his ability and experience.

There is room, however, for fruitful collaboration between the colleges, the hospitals, and the universities, and it would be a tragedy if this were not maintained.

In the first place, as the colleges have wisely recognised, a surgeon needs a more thorough knowledge of anatomy, physiology, and pathology than he obtained as an undergraduate, and the universities can cater for this need.

Secondly, it is, or should be, of great advantage for trainees, especially those who hope to join the staff of a teaching hospital whether in a full-time or a part-time capacity, to spend part of their postgraduate apprenticeship in a university surgical unit. As a general rule this should, I believe, be a unit which is responsible for undergraduate teaching, partly because the opportunity to teach also at postgraduate level is a great stimu to members of the unit, and partly because it is for the trainee to do some teaching himself.

What of courses of instruction in surgery? speak from experience because I have never let alone conducted, a formal course of postgraduate instruction, but I have an uneasy feeling that such courses are often regarded by fellowship candidates merely as short-cuts which will help them to pass their examination If this danger can be avoided, a well-planned course may be of real value, but no amount of formal instruction is an adequate substitute for practical experience

RESEARCH

A surgeon may undertake research with the object of advancing his own subject by developing new methods of diagnosis and treatment Alternatively, he may seize the opportunities which often arise in surgical practice of making new discoveries in anatomy, physiology, or pathology

In both types of research close liaison between the wards and the laboratory is of fundamental importance Indeed all the really great advances in surgery—such as the control of infection by antisepsis, asepsis, chemotherapy, and antibiotics, the use of blood transfusion and the discovery of accurate methods for controlling fluid and electrolyte balance, and the development of appropriate operations for treating lesions of almost every part of the body—have been brought about by combined clinical and laboratory research or by the clinical application of laboratory discoveries So swiftly has discovery followed discovery, however, that today a gap—one might almost say an iron curtain—has developed between the clinician and the laboratory worker, and each finds the language of the other almost incomprehensible

This gap can be bridged only by men with an interest in, and preferably first hand experience of, both fields Such men are rare and, perhaps on that account, often considered eccentric They are, however, in the authentic Hunterian tradition, for John Hunter—let us never forget—was both a surgeon and an experimental biologist It is, I believe, one of the important duties of a university clinical unit to guard this tradition and to provide an environment in which those who seek to follow it can flourish.

Summary

What I have tried to show may be summarised quite briefly It is, firstly, that surgery as a subject is a proper one for university study, and, secondly, that surgery as a profession needs men and women with knowledge and skill, and with that breadth of outlook which can come from university education at its highest level

I gratefully acknowledge the permission of the authors and the respective publisher or editor, to quote the words of Dr Ashby Professor Montrose and Sir Harold Himsworth.

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“ The welfare state has emerged by an evolutionary process in the sphere of social affairs but without sufficient education (or propaganda) to take the people along with all its implications The general attitude is unfortunately that of *taking* out of the national pool and putting nothing back There are obviously circumstances where only the resources of the State can provide complicated treatment or care over a long period for gross abnormality of physical or mental health Even here, as suggested earlier more could be done to help parents to accept responsibility for home care, encouraging them to overcome their trouble by living with it instead of passing it on to someone and somewhere else Put this way and remembering that it ’ is a child in trouble the rôle of the State should be more clearly that of a friendly adviser rather than providing a plain van to take difficulties away —ALAN MONCRIEFF *Child Health and the State* 1953, p 45

THE SUPRAPUBIC CATHETER

A METHOD OF TREATING URINARY RETENTION

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PUNCTURE of the distended bladder through the abdominal wall has many advantages but has always been regarded as dangerous If the puncturing instrument enters the peritoneal cavity it may damage the bowel or the omentum, while leakage of urine along its track may give rise to prevesical extravasation of urine and spreading cellulitis Either of these complications may be fatal

In 1943 Riches described a method of treating urinary retention caused by injuries to the spinal cord He devised an instrument by which a small rubber catheter could be inserted into the bladder by a stab through the skin and linea alba In 1949 he advocated the same technique for chronic urinary retention due to prostatic obstruction, but gave no details.

During the past three years this method of suprapubic catheter drainage has been used in almost all types of urinary retention coming under our care, whether due to acute or chronic obstruction or paralysis This paper contains a review of 150 consecutive cases

The Urethral Catheter

From time immemorial the relief of urinary obstruction has been by the passage of a urethral catheter If urine fails to make its way along the natural channel, it is rational to reopen the passage by the use of a curved and hollow tube Such, indeed, was the treatment until the end of the 19th century, when, through the work of McGill of Leeds and Freyer of London, suprapubic removal of obstructing tissue became an established and successful operation Thereafter, as the technique of prostatectomy became surer and safer, the catheter was used less and less Its use is still necessary before operation when urinary retention is present, and it is essential after operation while the bladder and prostatic capsule are healing

But the urethral catheter can be a troublesome instrument It cannot with certainty be retained in the urethra of a restless and mentally confused patient, it is recognised as the prime source of infection of the urinary tract, with all the serious or disastrous consequences, it is a cause of irritation and discomfort to the patient, and on occasion it is very difficult, if not impossible, to pass.

Some say that the catheter should not in any circumstances be used before operation, and that the correct way to treat urinary retention is to relieve the obstruction forthwith This surely is a counsel of perfection It presupposes a fully equipped urological unit capable of giving a twenty-four hour service including radiology and if need be biochemistry At present it can be achieved only by the few Secondly, and more important, it assumes that all such patients admitted to hospital are fit for major surgery In our experience this is far from true

The use of the suprapubic catheter to relieve urinary retention obviates to a large extent the difficulties inherent in the urethral catheter it is safe, the technique is simple, and the patient suffers only the slightest disturbance At any time subsequently the patient can undergo an operation to relieve the obstruction, or, should he be considered permanently unfit for a major surgical operation, the catheter can be retained or a larger one substituted.

Technique of Puncture

On admission to the ward the patient is examined and, if he is in pain, morphine is given The catheter

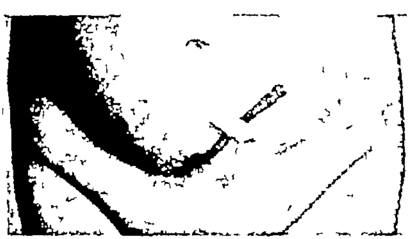

Fig. 1—Urinary retention treated by suprapubic catheterisation in patient aged 75 Wound is 3 in. above symphysis pubis.

s then introduced under local anæsthesia with the atient in his bed in the ward Several points need mphasis.

To define the size and outline of the bladder, percus ion, the customary method, is unreliable. In acute etention the circumference of the tense bladder can ily be felt after the protective spasm of the abdominal uscles has been relaxed with morphine. In chronic or aralytic retention the bladder is often larger, and no ifficulty has been experienced in palpating its outline A point on the skin is then chosen 1 inch below the level t which the anterior surface of the bladder curves ackwards to the superior It has, however, not been ound to be of any value to have the site of entry more han about 3 inches above the pubes (fig 1)

The question may fairly be asked how often is the eritoneum penetrated or bowel or omentum damaged ?

Anatomically the procedure appears to be safe. Rogers (1952) describes the peritoneal reflection on the anterior urface of the bladder in the following words :

> "When the fundus of the bladder is 2 inches above the pubes the peritoneal reflection is probably not more than /4 inch above the same bone When the fundus of the bladder s midway between the umbilicus and the pubes there may be 2 inches of the anterior abdominal wall in the middle line and immediately above the symphysis devoid of peritoneal lining Thus it happens that the distended viscus may be readily tapped above the pubes without the peritoneum being wounded."

This suggests that, when the bladder is enlarged up to, or almost up to the umbilicus, as in almost all our cases some 3 inches or more of bladder is free from peritoneal covering above the symphysis pubis.

But experience is more eloquent. In 150 cases no complication has arisen by damage to peritoneal contents. Moreover 89 of these cases were treated by house-surgeons whose experience in operating was negligible and to whom the technique had been demonstrated but once or twice

In some cases at operation or at necropsy it has been found that the lowest fold of peritoneum consisting of two apposed surfaces lying on the distended anterior bladder wall, has been perforated The significance of this will be discussed later

When the catheter is being introduced, it has proved necessary not only to make a small vertical incision in the skin 1/4–1/2 inch in length but also to cut through the strong fibrous tissue of the linea alba to the same extent. If this is not done, the catheter may be torn from the instrument while it is being introduced.

Position of Catheter

After the catheter on its introducer has been carried past the linea alba on to the bladder surface a short sharp stab is made with due warning to the patient that he will feel momentary pain or discomfort. A boring movement must not be used, for it tends to drag the catheter off the introducer or to dissect the layers of the bladder wall one from another so increasing the likelihood of bleeding

With the catheter in the bladder the introducer is removed and the advancer inserted. The catheter is then pushed onward to the bottom of the bladder at a point just behind the trigone (fig 2) This is an important step The catheter should be well down otherwise, when the bladder contracts on emptying (fig 3) the open end may be drawn up to or out of the wall with consequent likelihood of a leak of urine into the prevesical tissues.

A 'Nylon' stitch is used to secure the catheter to the skin and this is reinforced with adhesive strapping We have learnt that in a restless patient the shield devised and illustrated by Riches is insufficient to hold the catheter in position.

In several cases the track of the catheter has been dissected when prostatectomy was performed, or at necropsy After traversing the abdominal wall at right angles to the skin surface the catheter passes through the prevesical fat to a point on the anterior aspect of the bladder which varies with the degree of its distension When the bladder is empty the catheter enters below the level of the top of the symphysis pubis (fig 3) If the bladder is filled, its wall slides up the catheter, reducing the length of its extravesical course and increasing the length which remains inside the bladder

Extravesical Leak of Fluid

Of the 150 cases in this review some degree of urinary leak outside the bladder has been noted in only 2 In

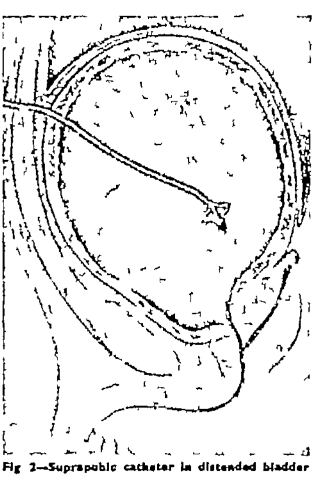

Fig 2—Suprapubic catheter in distended bladder

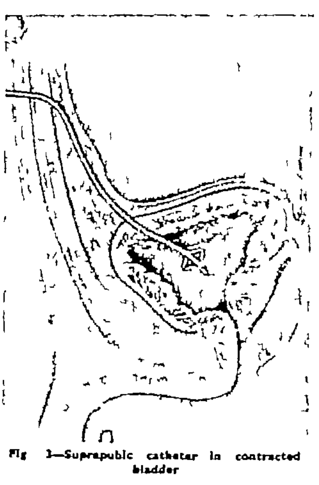

Fig 3—Suprapubic catheter in contracted bladder

the first the abdominal wall was dissected in the way described for the standard operation of suprapubic cystostomy, leakage took place because the hole into the bladder was too large In the second the catheter was apparently pulled almost out of the bladder In each case the tissues were œdematous and difficult to handle when prostatectomy was done, and adequate exposure of the bladder was much impeded

No case of extensive urinary extravasation or of spreading cellulitis has been seen, but a little prevesical œdema is sometimes found

Choice of Patient

Since Sept 1, 1949, suprapubic catheterisation has been used with increasing confidence and frequency Between this date and January, 1953, 233 cases of acute or chronic urinary retention have come under our care 150 were treated by suprapubic catheterisation, while 83 were treated by other methods or did not require treatment

	No of cases
Indwelling urethral catheter	58
Relieved spontaneously	10
Immediate prostatectomy	5
Moribund no treatment	4
Dilatation of stricture	3
Immediate suprapubic cystostomy	2
Cystodiathermy of papilloma	1
	83

The group treated by urethral catheterisation was largely composed of three types of case (1) those admitted to, or developing retention in, another ward in the hospital, (2) those known or suspected to have carcinoma of the prostate, and (3) those in whom some local anatomical reason precluded the use of the suprapubic catheter

As our experience has increased, the urethral catheter has been used less There are, nevertheless, certain cases in which its continued use is advisable or essential

(1) When a young patient develops urinary retention during an attack of pneumonia or congestive heart-failure, and the disease is not serious enough to keep him in bed more than a few days, it is better to use a urethral catheter This turn of events is not uncommon An indwelling urethral catheter is tied in, but removed as soon as the patient can get out of bed and walk Normal micturition then returns

On the other hand, some of our most rewarding cases have been in older men desperately ill in a medical ward whose retention has been relieved by suprapubic catheterisation and who, some four or six weeks later, have been fit enough for prostatectomy

When the bladder has to be drained for a long time the use of a urethral catheter too readily leads to infection, we prefer to resort to suprapubic drainage

(2) Suprapubic catheterisation has hitherto been thought inadvisable in patients with prostatic carcinoma Many such patients respond well to œstrogens with or without a short period of urethral catheterisation Others require endoscopic resection Our fear has been that in cases of carcinoma, suprapubic drainage of the distended bladder may lead to a permanent fistula, but it is probably unfounded We have not seen any case of fistula, and the wound usually closes with astonishing rapidity

(3) Where there is no free access to the anterior bladder wall or where the tissues are infected, suprapubic catheterisation should not be used For instance, when the peritoneal cavity has been drained suprapubically for peritonitis the scar may prevent the peritoneal fold from rising with the bladder as it distends This is usually obvious on palpation The bladder lies away from the abdominal wall, and the scar acts as a warning As an example of infection, a man was admitted with retention of urine and a cellulitis *of the lower abdominal* wall A urethral catheter was used He was subsequently found to have a breaking down vesical carcinoma.

Results of Treatment

After the initial relief of urinary obstruction the patient's general condition is assessed and further investigations are made The disposal of 150 cases after preliminary treatment by suprapubic catheterisation was

	No of cases
Prostatectomy	87
Urethral dilatation for stricture	5
Suprapubic cystostomy	23
Relieved without further treatment	12
Died without further treatment	23
	150

A few words of explanation must be said about each group

PROSTATECTOMY

When prostatectomy is to be performed the diagnosis is confirmed by cystoscopy immediately before the operation If a suprapubic rather than a urethral catheter has been used, the urethra will be uninfected and the bladder base will not have been irritated by an indwelling catheter No traumatic or infective œdema will obscure the field, and the state of the trigone and surrounding tissues can be readily judged

If prostatectomy is indicated, the suprapubic catheter is removed and the operation of choice is done A midline incision is made from the site of entry of the catheter to the symphysis pubis No attempt is made to search for and to close the hole in the bladder through which the catheter passed, this has been found to be unnecessary

In retropubic prostatectomy the approach is unimpaired If a transvesical operation is performed, the bladder may be contracted and difficult to distend in the same way as it is after long continued drainage by urethral catheter But this is by no means invariable, even when the catheter has been in for several weeks.

The choice of operation is in part a matter of personal preference and experience The type of prostatectomy done was as follows

	No of cases
Retropubic enucleation	55
Transvesical enucleation	25
Endoscopic resection	7
	87

A retropubic operation was usually chosen for the fit active men, and the transvesical approach with suprapubic drainage for the old and frail It was, of course, in the latter that prolonged catheter drainage was necessary The perurethral method was used in cases of carcinoma or where prostatic enlargement was slight

The length of time the suprapubic catheter was retained before operation is shown in the accompanying table

Catheter retained (days)	Retropubic enucleation	Transvesical enucleation	Endoscopic resection	Total
1–5	28	7	2	37
6–10	22	6	1	29
11–15	2	4		6
16–20	1	1	1	3
21 or more	2	7	3	12
	55	25	7	87

URETHRAL DILATATION

This was done in the operating theatre as soon as a stricture was diagnosed The suprapubic catheter was then spigoted, and the patient instructed to pass his urine in the normal way The catheter was removed forty eight hours later, urine seldom leaked, and then only in the first few hours

SUPRAPUBIC CYSTOTOMY

n the early days this operation was performed either en it was clear that prostatectomy never could be ie—e.g., in a patient already suffering from gastric rcinoma—or where fitness for operation was improbable thin a month With experience however we have nd fewer indications for its use It is in itself almost serious as a quick enucleation of the prostate and our 23 patients 8 died within a few days of the ration.

In addition the suprapubic catheter can be retained several months and provides quite adequate bladder ainage After two or three weeks the original catheter y be superseded by a straight soft rubber urethral theter as described by Riches it is inserted immedi ly *after removal of the first.* *We have found it advis*le to keep the patient in hospital during this waiting riod There still remain a few patients who because ey refuse operation or because an interval of two or ree months is deemed advisable, will return home with e large de Pezzer catheter for bladder drainage

RELIEVED WITHOUT FURTHER TREATMENT

In this group are those patients with negligible prostatic largement or congestion who need no surgical relief stoscopy establishes the diagnosis, and thereafter e suprapubic catheter is spigoted and normal micturi n returns.

There were 2 cases of paralytic distension in one bes dorsalis was diagnosed after the retention had been lieved in the other, paraplegia was caused by a mour of the spinal cord. In both cases normal micturi n was regained after treatment of the primary disorder

DIED WITHOUT FURTHER TREATMENT

The figure of 23 may well be considered large, but alysis shows that in most of them urinary retention s merely an incident in the life of a patient already ill dying from a serious medical disorder The relief of tention was essential for the patient's comfort, but ntinued decline was inevitable

It is in such cases that the suprapubic catheter is a on. It is easily inserted and when in position it causes e patient no discomfort It can be retained indefinitely d seldom needs attention apart from periodic changing n our experience it is far less often pulled out than an dwelling urethral catheter

In 16 of the 23 cases the primary cause of death was related to the urinary condition as follows heartilure (4 cases) pneumonia (4) cerebral hæmorrhage (3) ulmonary tuberculosis (2), paraplegia (2, caries and condary carcinoma) and pulmonary embolus (1) All ese patients died within a month of admission

2 patients died from uræmia one within forty eight ours of admission (blood urea 254 mg per 100 ml.) d the other, after a fortnight, with a blood urea level hich never fell below 400 mg per 100 ml.

Of the remaining 5 fatal cases some incident relating o catheterisation may be considered partly responsible r death In 1 patient, aged 85 a urethral catheter was peatedly pulled out, and he died from pyelonephritis wo days after suprapubic catheterisation the suprapubic catheter should have been used on admission In 2 others, aged 78 and 83, the suprapubic catheter came out after they had been sent home. Both died from pyelonephritis after retention of urine had recurred either should have gone home at that stage. In a 4th ged 87 the catheter was reinserted by a male nurse ho failed to reach the bladder peritonitis followed ore precise details are not known, but it is clear that the reinsertion of a suprapubic catheter is a skilled task and must be done at once In the last a man aged 74 already in uræmia (blood urea 169 mg per 100 ml) died from pyelonephritis because of blocking of the catheter, which was not adequately cleared

Complications of Suprapubic Catheterisation

In the present series complications have been remarkably few, and all can be overcome

Displacement of the catheter is the commonest through inadequate methods of tying in, the catheter slips out. If this happens and urinary retention has recurred the catheter may be reinserted by the same technique as was used for its first introduction. If the accident is recognised as soon as it has happened, a urethral catheter can be inserted down the track and into the bladder without difficulty If the track cannot be found a urethral catheter must be used rather than allow retention to recur with the possibility of an ascending urinary infection.

Epididymo-orchitis has been seen once. This was in a patient whose prostatectomy was delayed because of severe acute asthma and bronchitis During his convalescence his catheter was spigoted and he was encouraged to try to pass urine normally A bilateral infection ensued

Urinary extravasation has been seen in 2 cases, as mentioned above, and is explained by a technical error in introducing or managing the catheter There has been no case of spreading cellulitis or prevesical suppuration even where the catheter had to be reintroduced after slipping out.

Peritoneal perforation is known to occur occasionally (we have seen it on 6 occasions) but provided the outline of the bladder is carefully determined before the catheter is introduced no trouble arises from damage to bowel or to omentum (a complication which we have not seen) The fact that a portion of the catheter passes through the peritoneal cavity appears to be of no significance, though of course it is undesirable that it should do so If the bladder can be felt lying against the anterior abdominal wall introduction of a suprapubic catheter is safe

Hæmorrhage to a mild degree usually follows introduction of the catheter occasionally it is moderate No retention of urine was observed but a clot 2 inches in diameter was found in the bladder of a man who died from bronchiectasis and bronchopneumonia. Retained clot should be evacuated by cystoscope and suction.

Conclusions

Suprapubic catheterisation for treatment of acute and chronic urinary retention has been tried in 150 cases It has proved safe and simple Minor modifications have been made in the technique first described by Riches

It has definite advantages over the urethral catheter It is more comfortable because the patient can get out of bed and walk about remaining up all day Infective complications are reduced and there is no urethritis It does not interfere with the subsequent treatment of obstruction of the bladder neck or of the urethra by whatever technique is considered desirable Cystoscopy is made easier and more accurate. Finally the opinion of the ward sister and nurses is convincing—the patients are more contented and easier to nurse

Thanks must be accorded to Mr H G Hanley in whose unit and under whose inspiration this work was done It would have been impossible without the coöperation of a succession of enthusiastic and able house surgeons. I am grateful also to Mrs. Freda Wadsworth for her drawings, and Mr E Stride A.I.M.P for the photograph.

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ICTERUS OF THE BRAIN IN THE NEWBORN

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Yellow pigmentation of the brain is a striking complication in some cases of neonatal jaundice Although this pigmentation is not always confined to the nuclear masses, the term kernicterus or nuclear jaundice seems to be applied to any type of brain jaundice in which the nuclei are chiefly involved

The experience of one of us (Claireaux 1950) seemed to suggest that the condition was invariably associated with *icterus gravis neonatorum resulting from* hæmolytic disease Similarly, Potter (1952) stated that she had never observed icterus of the brain complicating conditions other than erythroblastosis Nevertheless the work of Aidin et al (1950), Zuelzer and Mudgett (1950), and Govan and Scott (1953) showed that nuclear jaundice was not uncommonly found in infants in whom the effects of rhesus iso immunisation could be excluded Indeed, Aidin et al remarked that, far from being the only cause of nuclear jaundice, hæmolytic disease was not even the commonest, they found nuclear jaundice in 16 6% of premature infants who came to necropsy

For this reason we have inquired into the incidence of both types of icterus of the brain in 376 necropsies of liveborn infants at Queen Charlotte's Maternity Hospital and Hammersmith Hospital during the five years 1948–52

A further problem of great importance is the nature of the pigment responsible for the yellow staining of the brain The suggestion has been made (Pickles 1949, Küster and Krings 1950) that this pigment may be the cause of brain damage Dereymaeker (1949) found that the staining reactions and solubilities of this pigment were those of bilirubin However, the assertion of Schmorl (1904) that staining was due to an abnormal pigment has been renewed by Bevis (1952b), who states that the pigment is mesobilifuscin arising from an underlying metabolic disorder

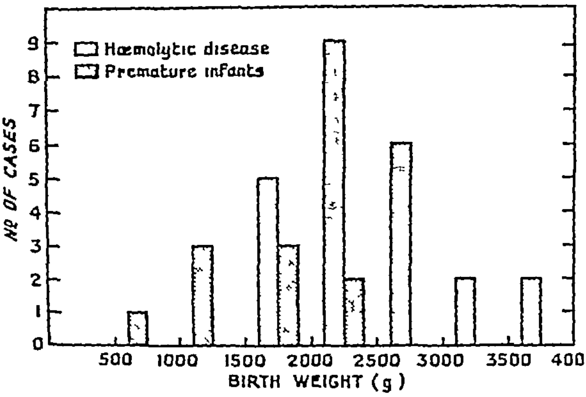

Fig 1—Distribution of birth weights among 9 babies with brain icterus associated with prematurity and 24 babies with brain icterus associated disease.

As a preliminary step in the investigation of the brain pigment Cole and Lathe (1953) have described a chromatographic method of fractionating bile pigments This method has now been applied to the study of the brain pigments in four cases of icterus of the brain, and to the examination of the serum pigments to which the brain is exposed in hæmolytic disease of the newborn

INCIDENCE OF BRAIN JAUNDICE

During 1948–52 at Queen Charlotte's Maternity Hospital and at the Institute of Obstetrics and Gynæcology, Hammersmith Hospital, there were 376 necropsies of liveborn infants Among these there were 33 cases of brain jaundice (8 8%) Of these 33 cases 24 (73%) showed evidence of rhesus iso immunisation, the remaining 9 were all premature infants in whom no evidence of rhesus incompatibility was found Of the 24 cases of hæmolytic disease 13 were males and 11 females, of the 9 other cases 6 were males and 3 females.

MATURITY OF INFANTS

The birth weight of the infants with hæmolytic disease was partly determined by the fact that pregnancy was terminated spontaneously or electively in all but 3 cases, most of them at 36–38 weeks' gestation One pair of affected twins of 34 weeks' gestation is included. The distribution of the birth weights of this group of infants is shown in fig 1

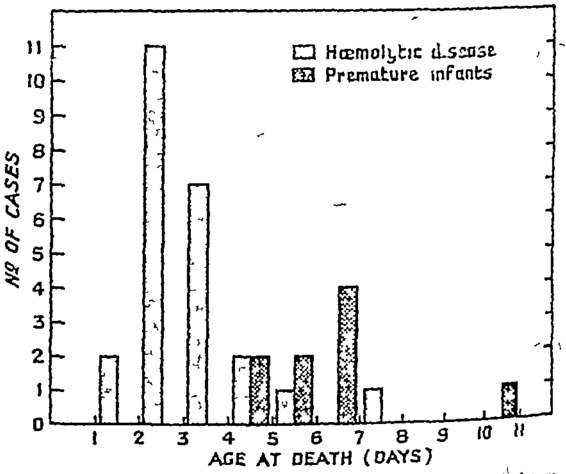

Fig 2—Distribution of age at death among 9 babies with brain icterus associated with prematurity and 24 babies with brain icterus associated with hæmolytic disease.

The other group of infants were all premature with birth weights well under 2500 g (fig 1) One infant weighing 640 g was delivered spontaneously at 28 weeks There were three twins in this group Their partners had also been jaundiced after birth but recovered.

TIME OF DEATH

There was a striking difference between the two groups. The infants with hæmolytic disease seldom survived more than four days, but no infant of the premature group died before the fifth day (fig 2)

CLINICAL FEATURES IN THE INFANT

All the infants with hæmolytic disease were rhesus positive and gave a positive Coombs test The hæmoglobin level of the blood varied from 24% to 140% (Haldane) Red blood-cells varied from 1,900,000 to 5,500,000 per c mm All the infants had moderate to severe jaundice which appeared within the first two days The liver and spleen were enlarged in 11 cases, the spleen alone in 8 cases, and in the remaining 5 no enlargement was found. In 12 cases an exchange od transfusion was given and in 3 cases a simple ect blood transfusion was given In 1 case an exchange nsfusion was attempted but failed In the remaining ases no transfusion was given. In these 8 cases the moglobin level was well over 100% and varied from to 140% (Haldane)

of the 9 premature infants were rhesus positive and as rhesus-negative, in 4 no information is available e Coombs test was negative in all 9 infants. The depth jaundice varied considerably There was 1 case of pato-splenomegaly 1 infant had gastric and pul nary hæmorrhage, 1 was deeply jaundiced and eloped peritonitis as a result of perforation of the um after an ileocæcal intussusception, 1 developed onchopneumonia; and the remaining 5 showed no usual features apart from jaundice. There were thus y 2 cases related to infection

CLINICAL FEATURES IN THE MOTHER

None of the 23 mothers of the infants with hæmolytic ease was a primipara, 10 of them were in their second gnancy, and 8 in their third. In 13 cases the prog ncy was terminated at the 36th–38th week because of molytic disease, this was done by artificial rupture the membranes in 10 cases and by elective cæsarean tion in 3 cases. Spontaneous labour took place at m in 2 cases at the 42nd week in 1 and before the th week in 7 All the pregnancies had been uneventful the 1 pregnancy which produced twins and terminated ontaneously at 34 weeks both twins were affected. All mothers were rhesus-negative and had antibodies in eir serum

Of the 9 mothers of the premature infants 5 were uniparæ 2 of them bore twins at 32 weeks gestation d 1 of these infants had acute hydramnios 1 had a vere antepartum hæmorrhage at the 32nd week and s delivered by cæsarean section, and 2 had uneventful egnancies. Of the 4 mothers who had previously borne ildren 1 had a twin pregnancy complicated by dramnios 1 had a slight antepartum hæmorrhage m a lateral placenta prævia 1 had an uneventful egnancy which was suddenly terminated at 26 weeks the spontaneous onset of labour, and 1 had an eventful pregnancy which terminated spontaneously 32 weeks. 7 of the mothers were rhesus positive, and one had antibodies in her serum. The incidence of normalities during pregnancy in this group was not gher than would be expected in any series of premature iveries.

Pigment in the Brain

The distribution of pigment in the brain was somewhat adable, and no distinction could be made between the o groups of cases. In 6 infants with hæmolytic disease d in 2 premature infants there was general diffuse ellow staining of the brain in addition to the nuclear gmentation. In 2 infants the periventricular white atter in the cerebrum was stained, and in 1 the peri queductal tissue was yellow In the remainder various uclear structures were involved.

CASE SUMMARIES

The pigment responsible for colouring the affected eas of the brain was extracted in 4 cases 2 in infants ith hæmolytic disease, and 2 in premature infants The nical and pathological findings in these cases were as llows

Case 1.—Male Birth weight 2732 g Spontaneous vertex livery at 37 weeks. The mother a 5 para aged 25 was esus-negative with antibodies. The infant was rhesus sitive and the Coombs test was positive. The blood moglobin was 107% (Haldane) Four days after delivery the baby developed head retraction and grunting respiration He died at the age of 5 days.

Necropsy showed jaundice hepatosplenomegaly intra lmonary hæmorrhage, and pale yellow staining of the basal nglia, olives, and medullary nuclei

Summary—Icterus gravis neonatorum with nuclear jaundice

Case 2.—Male Birth weight 2326 g Spontaneous breech delivery at 34 weeks. The mother, a unipara aged 29 was rhesus negative with antibodies. The infant was rhesus positive and the Coombs test was positive The blood hæmoglobin was 24% (Haldane) An exchange transfusion was given but the infant's condition steadily deteriorated and he died at the age of 50 hours

Necropsy showed intense jaundice hepatosplenomegaly intrapulmonary hæmorrhage and diffuse yellow staining of the whole cerebral parenchyma and intense jaundice of the basal ganglia, corpus Luysii cornu ammonis, and flocculus of the cerebellum

Summary—Icterus gravis neonatorum with diffuse cerebral icterus and nuclear jaundice

Case 3—Male Birth weight 1893 g Spontaneous vertex delivery at 34 weeks. The mother aged 19 was a primipara. The infant was jaundiced after twenty four hours but otherwise seemed well until the fifth day when he vomited collapsed suddenly with twitching movements, and died. His blood belonged to group A and was rhesus-positive Coombs test negative

Necropsy showed a deeply jaundiced premature infant, with no lesion in chest or abdomen, and with deep yellow staining of the periventricular white matter basal ganglia, cornu ammonis, vermis and flocculus of cerebellum, inferior olives nuclei in the pons, and nuclei in the floor of the 4th ventricle.

Summary—Premature infant with severe nuclear jaundice

Case 4—Male Birth weight 640 g Spontaneous delivery following sudden onset of labour at 26 weeks The mother was a unipara aged 33 The infant was pale at birth and a gradually deepening jaundice developed. A few convulsions were noted on the second day The child died at the age of 7 days

Necropsy showed an extremely premature jaundiced infant with yellow staining in the periventricular white matter thalami cornu ammonis, mid brain nuclei, nuclei in the floor of the 4th ventricle and medulla, and the inferior olives.

Summary—Prematurity with nuclear jaundice

BIOCHEMICAL METHODS

The following methods were used

Brain pigments were extracted by homogenising the tissue in five volumes of Analar methyl alcohol. The mixture was allowed to stand at room temperature for two to four hours, and a clear supernatant fluid was obtained by centrifuging This was stored at −12°C and a small amount of fine white precipitate which formed was filtered off

For the isolation of pigments from serum 0·18 vol. of saturated ammonium sulphate was added, with mixing followed by 2·5 vol. of absolute ethanol The turbid mixture stood for half an hour at room temperature before being centrifuged The clear supernatant fluid was decanted and stored at −12°C

The quantitative van den Bergh estimation was done in the usual way by adding to sera, or tissue extract, one-half volume of freshly diazotised sulphanilic acid and then three volumes of alcohol The depth of colour was estimated in a photo-electric colorimeter

Pigments from brain and serum were examined by the method of Cole and Lathe (1953) using reverse phase chromatography on silicone-treated kieselguhr and the solvent phases formed from 25 vol. chloroform 25 vol carbon tetrachloride 38 vol. methyl alcohol, and 12 vol 0·025M phosphate buffer It was found convenient to use 6 g of kieselguhr in glass tubes of 1·6 cm. internal diameter and 3 ml. of stationary phase The fractionation procedures reported here were all done under comparable conditions, and the results recorded as sketches of the chromatogram columns, showing the bands of pigment after 15 ml. of the mobile phase had come off the column. The columns of brain extract represented 4 g of brain, and those of serum were equivalent to 1·5 ml.

EXAMINATION OF PIGMENTS

Each of the four brains was treated in the same way but only that of case 2 is described in detail because only minor quantitative differences between the four specimens were observed. When the brain was sectioned at necropsy the deeply stained nuclear areas (9 g) were separated from the remainder of the brain (205 g) The intensely stained, circumscribed, areas probably amounted to less than 10% of the total "nuclear" fraction, because it was impossible to avoid including much unstained material with it The pigments were extracted from both parts of the brain—i.e, the separated "nuclei" and the "remainder" The total amount of diazo reacting material was equivalent to 2 mg of bilirubin per 100 g of the "nuclei" and 0 5 mg per 100 g in the "remainder" Presumably the concentration of pigment was from five to ten times as great in the small pigmented patches

Portions of the extract were taken to dryness in vacuo, and run on to reverse phase chromatograms in the mobile phase After 15 ml of solvent had run through the column, the position and size of the pigment bands from the extracts of the stained "nuclei" and of the "remainder" were noted and sketched (fig 3*a* and *b* respectively) Each chromatogram showed two yellow bands, the upper slowly moving band being substantially larger and much more intensely stained than the lower fast moving band In this respect the same general pattern was observed in both chromatograms, but a difference was observed in the size and tint of the upper band, which was wider and more deeply coloured on the chromatogram of the nuclear fraction

As an aid in identifying these bands 50 μg of bilirubin was run on another chromatography column under the same conditions, producing the result shown in fig 3*c* The bilirubin took up a position intermediate between the two bands from icteric brain However, when bilirubin was added to an extract of this brain, and the combined material was run on a column, the result (fig 3*d*) was similar to that of the nuclear extract (fig 3*a*), the bilirubin moving with the slow upper band, which it intensified

It was concluded that on the chromatogram the predominant pigment of brain icterus behaves identically with bilirubin in the presence of brain extract

To determine their van den Bergh reactions the pigments were eluted from the chromatography columns They gave positive diazo reactions, that of the upper band being much stronger than that of the lower band. This was in agreement with the relative depth of yellow

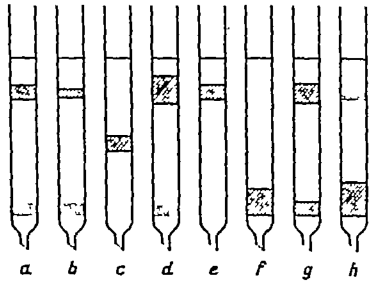

Fig 3—Appearance of standard chromatography columns

a, extract of "nuclear" portion of icteric brain, showing prominent slowly moving upper band of indirect reacting pigment, and faint lower band of fast-moving direct reacting pigment
b, extract of "remainder" of icteric brain
c, standard of bilirubin
d, bilirubin added to "nuclear" portion of icteric brain
e, bilirubin added to extract of normal brain
f, direct-reacting bile pigment added to extract of normal brain
g, extract of serum removed during exchange transfusion of infant with hæmolytic disease, showing greater proportion of lower fast moving direct reacting pigment than in icteric brain (*a*)
h, extract of serum from surviving jaundiced infant without hæmolytic disease, showing great predominance of lower fast moving direct reacting pigment.

For comparison, extracts were made of the brains of two babies who died of rhesus incompatibility at the ages of 3 and 15 hours There was no visible staining of the brain tissue The bile pigments in the serum of one of these babies were equivalent to 6 3 mg of bilirubin per 100 ml The colour of the brain extracts confirmed the lack of tissue staining The brains of five stillborn babies were also examined without finding any significant amount of pigment.

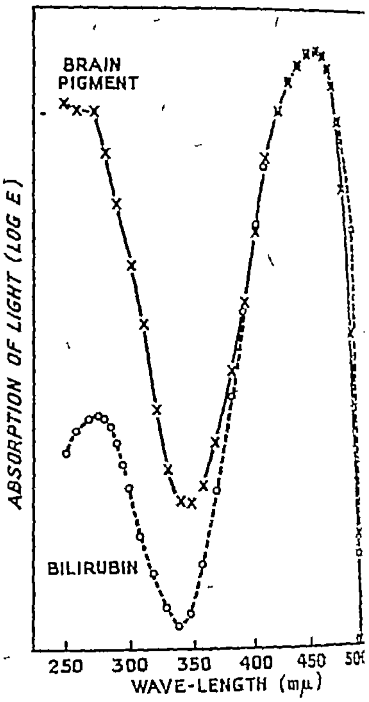

Fig. 4—Ultraviolet and visible spectrum absorpt curves of standard bilirubin and of brain pigm

Visual and Ultraviolet Absorption Curves

The character of the pigment present in brain icter was pursued further by studying its absorption cur This was examined in the solvent as it came off t partition column For comparison under identical co ditions a standard of bilirubin was also run through column In fig 4 the curves of the two pigments a compared They are almost identical throughout t visible range (400–510 mμ), but in the ultraviolet ran they differ, the brain pigment having a noticeably grea absorption This ultraviolet absorption, in excess of th of bilirubin, has also been observed when bilirubin h been put on the chromatogram with normal unstain serum extract, and in fact the corresponding eluates serum alone absorb in this region Accordingly t difference from bilirubin may be attributed to t materials which are eluted from the column with bi rubin In other respects the absorption characteri of the brain pigment are those of bilirubin, and they sh identical peaks at 454 mμ.

Pigments in Serum

Since staining of the brain takes place only when the is an excess of pigments in the serum, it may be assum that the brain pigments have their immediate origin the blood stream Hence it seemed important to obta information about the types of pigment to which t blood brain barrier is exposed In erythroblasto fœtalis it is possible to examine these pigments in t blood removed at exchange transfusion, and this w done in 9 cases by the same techniques as were appl to brain extracts It would have been preferable t compare brain pigments and serum pigments from t same patients, but in recent months only 1 pati undergoing exchange transfusions has died, and no bra icterus was present in this instance

The chromatographic examination of the 9 ser specimens from exchange transfusions revealed that upper slowly moving pigment, which is bilirubin, pr dominated in 8 cases, but there was a considerabl ation in the amount of the lower fast moving bile nent which reacts directly in the van den Bergh . In one of the exchange-transfusion sera this latter nent was present in larger amounts than was bilirubin, in several cases appreciable quantities were present 3g) Since this difference in pigment composition ween brain and serum suggested a selective con tration of bilirubin in the pigmented areas of brain er evidence of discrimination between these pigments looked for in tissue extracts

he sera of jaundiced newborn babies do not all show same proportion of pigments as was found in the d removed by exchange transfusions. In particular fast-moving direct reacting bile pigment may be far e abundant Recently we have seen 3 jaundiced new n infants of this type all having greatly increased unts of bile pigments in the serum (one had 50 mg 100 ml) but bilirubin was responsible for only a or part of this increase as a chromatogram of serum act showed (fig 3h) These babies survived.

Bilirubin retaining Lipid

n observation that appeared to throw some light on staining of brain tissue was the slowing of the rubin band on the column when an extract of icteric n was run simultaneously (fig 3*d*) The same effect demonstrable with extract of unstained brain . 3e) and with extracts of serum Since these chromato ms are partition columns the retardation of bilirubin t be due to either a relative increase in the volume of stationary phase or to an increased concentration in phase The first possibility was excluded by mining the effect of brain extract on the movement bilirubin and an eosin dye. Without brain extract y move at an almost identical rate In its presence ever, bilirubin is held back without the movement the eosin being affected. There is thus some specificity the affinity of brain extract for bilirubin

Whether the fast-moving direct-reacting bile pigment serum would be retarded was next determined. Some this pigment was obtained from the serum of an adult h obstructive jaundice and was added to an extract brain. Its rate of movement on the column (fig 3*f*) wed that the bilirubin retaining material had no nity for the direct-reacting bile pigment.

It was of some interest to see whether there were ater amounts of this bilirubin retaining material in mented than unpigmented brains, and more in nuclear ' areas than the remainder ' No differences re found, but this might be due to the method of imation, which is only semiquantitative, and to the ficulty of getting predominantly nuclear materials for aly From the position of the bilirubin retaining aterial on the columns a lipid character may be inferred, t large amounts of brain lecithin, cephalin, cerebroside, olesterol and neutral fat were inactive

DISCUSSION

In this survey *of cases from two hospitals it was* nd that jaundice of the brain occurred in about 1 per 00 live births and in almost 9% of neonatal deaths ere are certain pronounced differences between the o groups of infants who show icterus of the brain e first group is associated with hæmolytic disease of newborn the affected infants are usually mature, less the pregnancy has been deliberately interrupted ause of the hæmolytic disease. Their mothers are ost invariably multiparous since they most commonly elop iso immunisation as the result of a previous gnancy The infants may be jaundiced at birth or elop jaundice shortly afterwards. The greatest rtality is on the third day

By contrast the patient in the second group of cases is ally a premature infant. There is no evidence of rhesus iso immunisation in the mother most of the mothers in our series were rhesus positive. The mothers are often primiparæ, as this series shows since previous sensitisation is apparently not essential to the development of the lesion in this group The greatest mortality in this group is on the seventh day

In spite of these pronounced differences in the pathogenesis of icterus of the brain in the two groups of patients the general distribution of the pigment in the brain does not appear to differ from one group to the other

The brain pigment from 4 newborn infants representing both types of case has been examined. From a study of the diazo reaction, the chromatographic behaviour and the absorption spectrum we conclude that the brain pigment of each type of case is bilirubin.

Schmorl (1904) is sometimes cited as saying that the pigmentation in brain icterus was not due to bilirubin, and a similar argument has been advanced by Pickles (1949) It must be recalled that at the turn of the century little was known of the different bile pigments and as a result Schmorl spoke of jaundice being due to ' bile pigment He observed that the organs of newborn infants affected with nuclear jaundice remained yellow when preserved in formalin, whereas the organs from other cases of neonatal jaundice turned green. He concluded from this that the nuclear pigmentation was not due to ' bile pigment. However evidence that bile pigment ' was more complex was introduced a few years later by van den Bergh and Muller (1916) who noted that some icteric sera gave a direct diazo reaction and others gave an indirect reaction. These pigments have been separated by Cole and Lathe (1953) and it is clear now that the direct-reacting pigment, which moves fast on a chromatographic column, and predominates in obstructive jaundice is not bilirubin The indirect reacting pigment, characteristic of hæmolytic jaundice moves slowly on a column and is bilirubin. It has been known for a long time (van den Bergh 1918 Andrewes 1924) that the direct-reacting bile pigment is particularly easily oxidised to green derivatives, whereas the indirect-reacting pigment, now known to be bilirubin, is more stable Thus in the light of our present knowledge Schmorl s original observations are in keeping with the identification of the brain pigment as bilirubin

The claims of Bevis (1952a) that the yellow brown pigment of liquor amnii is mesobilifuscin and (Bevis 1952b) that this is also the pigment of icteric brain are difficult to assess without experimental evidence. In unpublished experiments we have fractionated samples of liquor amnii from patients with hæmolytic disease and found not one but several pigments. Unfortunately a specimen of mesobilifuscin has not been available for chromatographic comparison with the pigments from liquor amnii or for absorption studies in relation to brain pigment The absorption spectrum of mesobilifuscin (Meldolesi et al 1939) bears little resemblance to that of bilirubin. Moreover the nature of mesobilifuscin is very *obscure five types having been described by Siedel* et al. (1948) These workers who have been largely responsible for the studies of bilifuscins, state that mesobilifuscin does not give a diazo reaction (Siedel and Möller 1939) Unlike Bevis (1952b) we have found that the brain pigment reacts positively as does bilirubin.

In contrast to the brain extracts, in which bilirubin greatly predominated, extracts of serum from other cases of hæmolytic disease had a larger proportion of the direct-reacting bile pigment. Thus the brain seems to have a selective attraction for bilirubin. This possibility is supported by the demonstration that brain tissue contains a bilirubin retaining lipid, and that this material has no affinity for the direct-reacting bile pigment.

It is clear that the occurrence of extreme jaundice and of greatly increased quantities of bile pigments in the serum is not in itself necessarily damaging to the neonatal brain This is illustrated by the three newborn infants in whose serum the levels of total bile pigments were very high (up to 50 mg per 100 ml according to the diazo reaction) However, the amount of bile pigment present in the form of bilirubin was relatively small (fig 3*h*) From the survival of these babies it may be assumed that the direct reacting pigment did not affect the brain In a similar way it is possible to explain the anomaly that icterus of the brain does not appear in the more pronounced jaundice of adult patients with obstruction or in congenital atresia of the bile ducts in the newborn In these conditions the main pigment to which the brain is exposed is not bilirubin but the direct reacting bile pigment

Thus the relative absence of the direct-reacting bile pigment from icteric brain, together with the absence of brain icterus in clinical jaundice due to this pigment, serves to direct attention to the rôle of bilirubin in the production of brain icterus It follows, too, that the conversion of bilirubin to the direct reacting pigment tends to protect the neonatal brain from icterus There is much evidence from other sources that this change is made by the liver, and reduced liver function may contribute to the development of brain icterus in both types of case Indeed, a defect of this conversion may be the primary factor leading to the brain icterus of premature babies, in whom no increased production of bilirubin has yet been demonstrated. This would be consistent with the longer survival of the premature baby than of the baby with hæmolytic disease

These studies emphasise the crucial importance of bilirubin in the development of brain jaundice It now seems to be necessary to determine whether a high level of bilirubin has a direct toxic effect, or whether some additional factor—e g, cell damage, and altered permeability of the blood brain barrier—is a prerequisite for the development of icterus of the neonatal brain

Summary

The incidence of brain jaundice in neonatal infants in two large maternity hospitals has been determined.

About a quarter of the cases are associated with prematurity and clearly distinguished from the rest, which are associated with hæmolytic disease

The differences between these two groups of cases have been analysed

The pigment responsible for the staining has been extracted from the brains of two infants in each group The pigment of icteric brain in the premature infants is identical with that in the infants with hæmolytic disease It is bilirubin A bilirubin retaining lipid has been shown to be present in the brain

Direct reacting bile pigment is largely absent from the icteric brains but is present in various amounts in the serum of babies with hæmolytic disease This pigment is not concentrated by the bilirubin-retaining lipid of brain in vitro and it does not stain the brain tissue

Emphasis is laid on the rôles of bilirubin and of the liver, which may protect the brain of the newborn infant by converting bilirubin to direct reacting pigment

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YEASTS IN THE VAGINAL FLORA

THEIR INCIDENCE AND IMPORTANCE

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THRUSH of the vagina and vulva, caused by the yea like fungus *Candida albicans*, is well known, but les degrees of vulvovaginitis due to this organism ar probably inadequately recognised Investigations int the significance of vaginal yeasts have not been made i Britain, and surveys made elsewhere have often bee uncritical For these reasons we have assessed th incidence and significance of vaginal yeasts in patien attending four family-planning clinics in North Londo and Hertfordshire

Material and Methods

500 patients were examined All were attending th clinics for the first time, but 56 had attended a similar clinic on previous occasions and were regular users of contraceptive diaphragm New registrations include in the trial, on any one day, could not exceed 6, becau of the extra time required for questioning and for tak specimens New patients attending these clinics nev exceeded 10 in an evening and were often fewer than Postnatal clinics and general practitioners referred 1 patients, for instruction in birth control for medic reasons not pertaining to disease of the urogenit tract, the remaining 308 patients attended of their ow initiative None of the patients was known to be sub fertile, and of the 476 married ones 388 were parou Their ages ranged from 17 to 45 years The patient therefore comprised a selected section of the population although they included representatives from all five o the Registrar General's social classes (General Regist Office 1951)

One person took all the histories and made all th clinical observations throughout the investigation Mimeographed sheets were used for recording persona and medical histories, clinical observations, and laboratory findings The laboratory work was done withou knowledge of the clinical findings The data from the sheets were transferred to punch-cards for analysis.

HISTORY

Each patient was asked the same questions Th routine clinic questions dealt with general health an gynæcological, obstetrical, marital, and contracepti

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histories. Most patients did not volunteer information about gynaecological symptoms so it was necessary to elicit them by direct questioning Questions concerning pruritus vulvæ were the following:

(1) Have you ever had itching?
(2) Was this during pregnancy?
(3) Have you had itching during the last month, and is it present now?

Pruritus was recorded as mild unless the patient emphasised its severity It was recorded as present now, if the answer to either of questions (3) was 'Yes.' Parous patients were asked whether oral thrush had occurred in their children other questions dealt with douching and intravaginal tampons

CLINICAL SIGNS

These were recorded as soon as the patient had been examined and the laboratory material obtained. The presence or absence of vulval and vaginal inflammation was noted. The quantity of secretion or discharge was assessed as profuse moderate or scanty 'Moderate' and 'scanty' were considered to be within normal limits, but 'profuse' was regarded as pathological Its appearance was described as mucous, mucopurulent curdy or bloodstained The patient's description of the discharge was also recorded but bore little relation to our observations. For a clinical diagnosis of thrush the criteria were vaginitis and patchy white curdy, and rather adherent discharge, sometimes extending to the vulva and cervix. Cervicitis erosion, and ectropion were recorded with a diagram

COLLECTION OF LABORATORY MATERIALS

500 vulval and a similar number of vaginal swabs were examined With the patient in the lithotomy position a swab (previously soaked in Sabouraud's broth) was swept over the outer and inner surfaces of the labia minora and round the introitus. A sterile Cusco's speculum, without lubricant, was next inserted, the cervix was exposed and a second swab similarly soaked was passed round the outer surface of the cervix and into the posterior fornix. Finally, a pipette fitted with a rubber teat was inserted and 1 ml. of sterile 0 85% saline solution was ejected into the fluid in the vaginal pool After mixing some of this fluid was aspirated. Premarital patients were occasionally advised and in these cases, if the hymen was insufficiently dilated, the second swab was guided through a small sterile glass tube instead of through the speculum

LABORATORY PROCEDURES

The aspirates from the vaginal pool were examined within three hours for the presence of *Trichomonas vaginalis* Low power microscopy was used on the whole area of two wet preparations of each sample Since they could not be examined until morning the swabs for yeast investigation were stored overnight at 2°–5°C Quarter plates of Sabouraud's dextrose agar gentian violet bile salt medium (Littman) and penicillin streptomycin blood-agar (30 units of each antibiotic per ml. of medium) were inoculated from each swab Finally, the swab was used to make as thick a smear as possible over a circular area of half inch diameter on a slide. The smear was stained by Gram's method and examined for yeasts and pus cells before the results of culture were known. Each plate was incubated for forty-eight hours at 37°C and the amount of yeast growth was recorded as 0, 1–50 colonies, + ++ or +++ Throughout the survey the assessment of growth was made by one person. For identification a representative yeast colony was picked from each plate; where more than one type of colony was present each type was sampled Bacterial contaminants were excluded by plating on blood agar, and the yeast colonies were identified by the following cultural properties:

(1) The presence or absence of mycelium and chlamydospores, determined by deep streak culture in corn meal agar incubated at 22°C for forty-eight hours. When no mycelium was produced in corn meal agar potato water was inoculated

(2) The production of acid and gas in peptone water containing 2% glucose, maltose sucrose, and lactose

(3) The assimilation of carbohydrates (glucose maltose sucrose lactose and galactose) and nitrogenous compounds (ammonium sulphate potassium nitrate urea and asparagine by an auxanographic technique

(4) The production of ascospores on carrot slopes

Techniques for the differentiation of yeasts are fully described by Lodder and Kreger (1952) and a brief reference to the laboratory diagnosis of candida species is made by Riddell (1951) The production of chlamydospores is discussed by Gordon et al (1952)

Results

INCIDENCE OF YEAST LIKE FUNGI

Table I sets out the incidence of yeast-like fungi among the 57 patients from whom positive cultures were obtained *C albicans* was found in 38 of these the other yeasts comprised at least five species Most of the patients yielded positive cultures from both vulval and vaginal swabs, but 6 gave positives only from the vagina and 8 only from the vulva Of these, 4 and 5 respectively yielded cultures of *C albicans*

TABLE I—YEAST LIKE FUNGI IN VULVAL AND VAGINAL SWABS FROM 500 PATIENTS

Species	No of patients
Candida	
C albicans	38
C krusei	3
C tropicalis	3
C parakrusei	1
C mycoderma	1
Unclassified	3
Torulopsis (Cryptococcus):	
T glabrata	7†
Unclassified	2
Total	57

Including 6 cases of thrush.
† Including 1 patient also harbouring *C albicans*.

In smear preparations various species of yeast were found to be indistinguishable and the smear technique was shown to be useless as a guide to the presence of *C albicans* Although 9 swabs gave smears positive for yeasts which failed to grow in culture, smears indicated the presence of yeasts in only 66 of 102 swabs from which yeasts were ultimately grown

Of the 54 swabs giving profuse cultures 51 showed yeasts in the smear but the 48 swabs giving poor or moderate growths yielded only 15 positive smears (table II) For *C albicans* alone similar figures were obtained from 32 swabs giving profuse cultures positive smears were obtained in 20 instances; but 35 swabs which produced moderate or poor cultures gave positive smears in only 13

Sabouraud's dextrose agar as used in most laboratories was as satisfactory for primary isolation of yeasts as the other two media used in this investigation

TABLE II—COMPARISON OF CULTURES AND SMEARS FROM 1000 VULVAL AND VAGINAL SWABS

Species	Culture +++ and ++		Culture + and 1–50 colonies		Culture negative	
	No	With positive smear	No.	With positive smear	No.	With positive smear
C albicans	32	29	35	13	898	9
Other yeasts	22	22	13	2		
Total	54	51	48	15	898	9

TABLE III—RELATIONSHIP OF PRURITUS TO YEASTS

Pruritus	No of cases	With C albicans	With other yeasts
Severe	11	6	1*
Mild	72	7	5
Past history	139	8	5†
Absent	278	17	9
Total	500	38	20†‡

* *C albicans* also isolated from this patient
† Includes 1 patient in whom trichomonads were also present
‡ Includes 1 patient from whom *C albicans* was isolated

OTHER FINDINGS

Thrush was seen in 6 patients, and in each case *C albicans* was grown from both vulval and vaginal swabs In 4 of these patients both swabs produced heavy growths, but in the other 2 only moderate growths developed Yeasts were obvious in smears from 5 of these patients, but the 6th had scanty yeasts in the vulval smear and none in the vaginal one In the presence of an active infection with *C albicans* the greater reliability of culture technique is confirmed

Pruritus —Table III gives the incidence of pruritus and its relationship to the presence of *C albicans* A significant incidence of *C albicans* was found only in relation to severe pruritus (P<0 001)

Vulvitis, Vaginitis, and Cervicitis —Patients with vulvitis or with vaginitis harboured *C albicans* significantly more often than patients without these signs (P<0 001), but there was no significant difference in the incidence of "other yeasts" (table IV) Of 107 patients with vulvitis or vaginitis 21 harboured yeasts, of which 18 were *C albicans* Of 393 patients without these signs 37 harboured yeasts, of which 20 were *C albicans* There was no significant relationship between cervicitis and the presence of any yeasts

Vaginal Discharge —50 patients had a profuse discharge Thrush, present in 6 patients, was accompanied by profuse discharge in 3, and by moderate discharge in the other 3 There was a significantly higher incidence of *C albicans* in patients with a profuse discharge than in those with moderate or scanty discharge (P<0 05) (table V) *C albicans* accompanied a "curdy" discharge significantly more often than other yeasts (P<0 01)

Pus and Epithelial Cells in Smears —The numbers of pus cells were not significantly related to the cultural isolation of any yeasts

Duration of Marriage and of Parity —No significant relationship to either of these factors was observed 24 premarital women were examined, candida species were not isolated from any of them

Douching and Intravaginal Tampons —The incidence of *C albicans* was significantly higher in patients who douched regularly than in those who did not (P<0 05), no relationship could be shown between the incidence of yeasts and the use of intravaginal tampons (table VI)

TABLE IV—RELATIONSHIP OF VULVITIS, VAGINITIS, AND CERVICITIS TO YEASTS

Group	No of cases	With C albicans	With other yeasts
Vulvitis and vaginitis			
Vulvitis alone	44	6	0
Vaginitis alone	27	5	1
Vulvovaginitis	36	7	2*
Absent	393	20	17†
Total	500	38	20*†
Cervicitis			
Severe	64	6	2
Mild	174	13	5†
Absent	262	19	13
Total	500	38	20†

* Includes 1 patient from whom *C albicans* was isolated
† es 1 patient in whom trichomonads were also present.

Thrush in Infants —No correlation was found between the presence of *C albicans* and a history of thrush in the last infant The mothers' replies to direct questions were the only criteria of infantile thrush.

Social Status and Standard of Personal Hygiene —No significant relationship was observed between the factors and the presence of yeasts

Incidence of Trichomonads —Trichomonads were found in the secretions of 9 patients, from 1 of whom a yeast (*C tropicalis*) was grown None of these complained of pruritus during the past month, and only 1 had a profuse discharge There was, however, evidence of vulvovaginitis in 4 patients and of cervicitis in 3 None practised douching

Discussion

The incidence of yeasts in the vulvæ and vaginæ of this group of non-pregnant women was 11 4% (10 3% if thrush is excluded) Figures of other investigators for similar groups range from 7 3% (Weinstein and Wickerham 1938) to 15% (Carter and Jones 1937, Plass et al 1931) There is considerable evidence that yeasts occur more often in pregnant women, and figures for this group range from 25% (Weinstein and Wickerham 1938, Woodruff and Hesseltine 1938, Raurumo 1950) to 43% (Carter et al 1940) The species isolated in this survey are similar to those in other reports It is noteworthy that *C stellatoidea*, the vaginal strain described by Jones and Martin (1938), was not found among the 102 cultures isolated Rauramo (1950) also failed to isolate this organism from his cases The incidence of *C albicans* alone was 7 6% (6 5% if thrush is excluded) These figures are comparable with those obtained for similar groups by Negroni (1935) and Fisher and Arnold (1936) Their estimates of the incidence in pregnant women were three or four times as great

TABLE V—RELATIONSHIP OF VAGINAL DISCHARGE TO YEAST

Group	No of cases	With C albicans	With oth yeasts
Vaginal discharge			
Profuse	50	7	4*†
Moderate or scanty	450	31	16
Total	500	38	20*†
Vaginal exudate			
Curdy	51	12	2
Not curdy	449	26	18
Total	500	38	20

* Includes 1 patient from whom *C albicans* was isolated.
† Includes 1 patient in whom trichomonads were also present.

The infectivity of *C albicans* (syn *C pinoyi* and *C* *metalondinensis*) cultures inserted into the vaginæ of both pregnant and non-pregnant patients was shown by Hesseltine et al (1934) and Bland et al (1937), using other candida species for controls Bland et al showed that pruritus and increased discharge began twenty-fou to ninety six hours after inoculation In the presen study close associations were found between the presen of *C albicans* on the one hand, and vulvovaginit discharge (both profuse and curdy), and severe prurit on the other However, 14 of the 38 patients harbouring *C albicans* had neither signs nor symptoms This suggests that infection may be completely latent, mildly inflammatory (with or without symptoms), or the cause of full clinical thrush with symptoms of variable severity The response of the patient to the presence of *C albicans* is governed by factors which are at presen unknown

VI—RELATIONSHIP OF DOUCHING AND INTRAVAGINAL TAMPONS TO YEASTS

Group	No. of cases	With C albicans	With other yeasts
ng			
than once monthly	60	10	0
than once monthly	67	7	0
r	373	21	20
otal	500	38	20
ginal tampons			
	128	5	1
used	372	33	19
otal	500	38	20

ical assessment of purulent discharges was often ading Epithelial cells in smears from these often y exceeded pus cells in number and the latter were imes absent. C albicans did not tend to produce lominantly leucocytic exudate

ture for C albicans was positive in 6 of the 11 its with severe pruritus and all 6 showed profuse h. Of 72 patients with mild pruritus only 4 uding 3 cases of thrush) grew C albicans Smears s cells and trichomonads did not indicate bacterial otozoal infections The lack of correlation between pruritus and isolation of this yeast could possibly ie to the technique of direct questioning Very degrees of pruritus caused by the mechanical s of clothing or dried secretions, may thus have been led.

Family Planning Association clinics, patients do not teer information about discharges or pruritus, and ently very few had even consulted their general tioners. It appears that minor discomfort is ted by many women without medical advice being it.

is attitude in women with mild symptoms and nal signs, and the complete absence of symptoms igns in others harbouring C albicans, may prevent ynæcologist from taking special precautions as he d do in a case of obvious thrush If adequate aseptic iques are not observed, the organism can clearly be ferred from patient to patient, and this hazard is derably greater in the case of pregnant patients. ar comments in respect of trichomonads have been by Donald (1952) Where lack of other facilities sitates reliance on antiseptics it must be remembered C albicans is resistant to some accepted bacterial eptics customarily used in many gynæcological s.

i interesting correlation exists between regular hing and the presence of C albicans The douching t appears unrelated to the presence or absence of itus Probably a predisposition to infection results mechanical or chemical trauma and disturbance of normal bacterial flora Antibiotics are known to ur the growth of fungi by disturbing the balance of ai commensal bacteria and it is conceivable that hing may do the same.

ie results of laboratory diagnosis show three distinct

) Only two thirds of the yeasts found by culture may be bicans

) Species of yeasts cannot be identified from smears or ial appearance.

) Smears alone may show the presence of yeasts in only it two thirds of patients whom culture shows to be ouring C albicans

his survey shows that in clinically recognisable thrush h smears and cultures are positive. In such cases tment would probably be started on clinical grounds e. When cases of pruritus and leucorrhœa without frank thrush are being investigated, a smear or a single culture may be misleading C albicans may be reported when subsequent fermentation reactions would reveal some other species of yeast. If the gynæcologist suspects that a clinical abnormality is causally associated with the presence of C albicans, the following procedure is suggested

(1) Swabs of vulva and vagina should be cultured on Sabouraud's dextrose agar

(2) Pure cultures of yeasts obtained should be examined for ability to ferment peptone water containing 2% of sugar (glucose maltose, sucrose, and lactose) C albicans ferments glucose and maltose, forming acid and gas and sucrose forming acid only 2% sugar solutions are generally considered preferable but the 1% solutions available in most laboratories may be used

(3) Identification is completed by ascertaining the ability to produce chlamydospores. Some strains, however do so with difficulty

Animal pathogenicity tests are unnecessary in routine work since there is no reliable evidence of the existence of different degrees of experimental pathogenicity of strains of C albicans

Summary

An investigation was made to determine the incidence of vaginal yeast-like fungi in patients attending four family planning clinics

Yeasts were cultured from 57 of 500 patients 38 of these patients harboured Candida albicans and the remainder at least 5 other species.

The superiority of cultural methods over the examination of smears is illustrated

In the 6 cases of clinically recognisable thrush smears were all positive and C albicans was cultured.

Patients with severe pruritus, vulvitis vaginitis, or profuse and curdy discharge harboured C albicans significantly more often than those without these symptoms and signs.

The incidence of C albicans was also higher in those who douched regularly

No significant relationship was found between the presence of yeasts and the social status or standard of personal hygiene of the patient, the duration of marriage, parity a history of thrush in the last infant the use of intravaginal tampons or the presence of cervicitis,

The hazards of cross infection by C albicans are discussed

Recommendations are made on laboratory diagnosis

We wish to thank all those in clinics and laboratories who helped in this study The statistical advice of Mr B Benjamin of the General Register Office, is acknowledged with gratitude as also is the technical assistance of Miss Y M Clayton, of the Institute of Dermatology

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HYDROCEPHALUS ASSOCIATED WITH DEFICIENCY OF VITAMIN A

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Although many factors have been implicated in the production of hydrocephalus, it has not been reported previously that a deficiency of vitamin A in the mother may determine the development of hydrocephalus in her offspring

The association of vitamin-A deficiency with xerophthalmia and changes in other epithelial tissues has long been recognised Observations on laboratory and domestic animals have also provided data which indicate that lesions of the central nervous system may arise as a concomitant of vitamin-A depletion Various explanations of these nervous lesions have been advanced The most popular view appears to have been that put forward by Mellanby (1938), who claimed that overgrowth of bone is the factor that injures the nervous system Unfortunately most of the experimental studies on the effect of vitamin A deficiency have suffered from an incomplete examination of the central nervous system The available information on the effects of vitamin-A deficiency in domestic animals is confined mainly to the symptoms and to examination of the peripheral nerves

The present study arose from an investigation by one of us (G E L) on the effect of subclinical vitamin-A deficiency on fertility and growth in a strain of inbred rabbits It was noted that, in some of the young born to does deficient in vitamin A, symptoms of nervous disorder appeared at various times after birth Radiological examination suggested that the underlying condition might be hydrocephalus, and this diagnosis proved to be correct

Experiments and Methods

16 young rabbits aged from two weeks to two months, were obtained from five different litters In three litters all the young (5, 5, and 3) have been examined, in the other two litters surviving young, not yet showing symptoms, await further investigation All 16 rabbits showed signs of lesions of the nervous system 14 were killed in this investigation and 2 others died from natural causes and were later examined

3 of the does belonged to an inbred strain of stock rabbits and were mated to males of the same strain, 1 of the other 2 females was from the inbred strain but belonged to a line which had been separated out for colour some years previously the remaining doe was an outbred animal and was mated with an outbred male, both of them being quite unrelated to the other strain

All 5 does had received a diet which contained no detectable carotene (provitamin A) for fourteen weeks before mating 1 received orally a small amount of vitamin A in arachis oil (150 i.u. per kg body weight per week) No supplement of vitamin A was given to the young after weaning The rabbits used as controls were progeny from similar does receiving the same diet with the addition of a supplement of vitamin A

Attention was first drawn to the condition by the appearance of signs of nervous disorder and a curious retraction of the head in one litter Clinical examination revealed signs of paralysis, particularly in the hind limbs

Subsequent investigation included radiological examination of the skull and vertebral column, and the injection of 'Dag' colloidal carbon into the ventricles during life Coronal sections of the head were prepared after deep freezing, the hinder part of the cerebellum and lower end of the fourth ventricle were exposed by cervical laminectomy, and frozen sections made transversely through the mid-brain and cerebral aqueduct at all levels were prepared and stained In addition the optic nerves and their surroundings were examined in all the animals

Numerous control rabbits of comparable ages were examined at every stage of the investigation

Findings

Radiography revealed an enlargement of the calvarium of the skull and a "beaten silver" appearance of the bone similar to that observed in human hydrocephalus. This finding led to a tentative diagnosis of hydrocephalus and was largely responsible for determining the methods by which the material was afterwards treated

In all the rabbits examination of the coronal sections of the cerebral hemispheres revealed gross dilatation of the lateral and third ventricles In some specimens the cortex and white matter were reduced to such an extremely thin layer lining the interior of the skull that it was surprising to find such a condition compatible not only with life but even with comparatively few clinical signs of hydrocephalus (fig 1) In 1 rabbit the brain tissue had herniated through the skull and formed a slight swelling under the skin

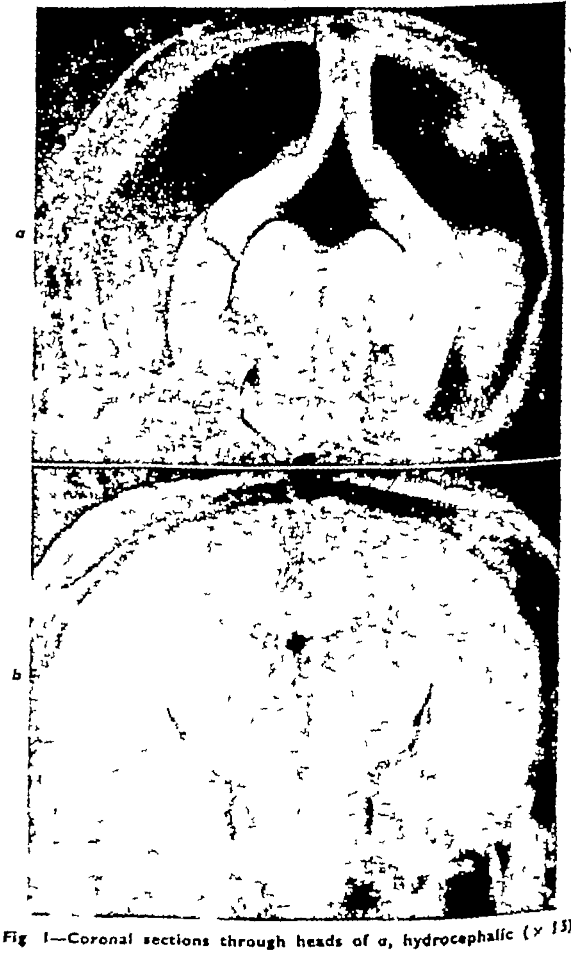

Fig 1—Coronal sections through heads of a, hydrocephalic (× 1½) and b normal rabbit (× 2½)

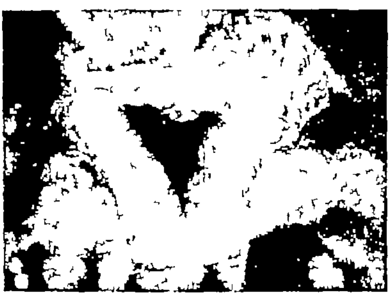

Fig. 2—Constriction of optic nerves in region of optic foramina of hydrocephalic rabbit (× 7 5)

Laminectomy showed that the cerebellum had herniated through the foramen magnum but the fourth ventricle appeared normal, and this was confirmed by subsequent microscopy In those animals in which colloidal carbon had been injected into the ventricles there was no sign of any carbon in the fourth ventricle, although the dilated lateral and third ventricles were well filled On further exposure of the brain and cranial nerves it was found that both optic nerves exhibited well marked constrictions at the optic foramina (fig 2) In none of the specimens was any deformity of the foramen magnum or of the base of the skull observed, nor was there any evidence of meningitis

The examination of *transverse sections through the* cerebral aqueduct revealed a well marked stenosis at the level of the superior colliculus Fig 3 shows transverse sections through the aqueducts of *a*, hydrocephalic and *b* normal rabbits The cross-sectional area of the lumen of the aqueduct in the hydrocephalic rabbit was 0·16 sq mm. and that of the normal rabbit 0 71 sq mm Above this level the lumen of the aqueduct was dilated and distal to the *constriction the aqueduct appeared* normal The colloidal carbon did not pass beyond the constriction.

In the absence of any figures for the size of the aqueduct in the normal rabbit comparison was made with sections through various comparable levels in control rabbits of corresponding age and size As a result of these investigations it was concluded that the signs of nervous disorder in these vitamin A deficient rabbits could be attributed to hydrocephalus produced by stenosis of the cerebral aqueduct. Further there appeared to be a causal relationship between the vitamin A deficiency and the development of the aqueductal stenosis.

Discussion

These findings introduce an entirely new concept of the ætiology of some forms of hydrocephalus.

The question naturally arises whether the hydrocephalus in these rabbits could be explained by a genetic factor Congenital hydrocephalus attributed to a genetic factor has been reported in mice (Grüneberg 1043, Clark 1034) It must be presumed that mutation was responsible for the appearance of these strains although no information is available about their diet. 14 of the present 16 rabbits belonged to a strain separated by Dr John Hammond in 1024 and inbred since then The characteristics of this strain have been carefully documented, and there is no record of spontaneous congenital hydrocephalus. It is considered that the finding of hydrocephalic young in five litters from different matings rules out the possibility of a mutation having been responsible for the condition Further of numerous control rabbits from the same strain none has ha hydrocephalus.

Because of its economic importance much attentio has been directed to the effects of vitamin A deficiency f farm animals

As long ago as 1910 Hart et al. noted that pigs fed o a deficient diet developed paralysis of the limbs. A necropsy the vertebral canal contained a considerab quantity of fluid, and in the spinal cord the anterior hor cells were shrunken, surrounded by fluid and appeared to b under pressure For some reason, however the brai though removed was not examined.

Mellanby working mainly on puppies, has contribute largely to the study of the effect of vitamin A deficienc on the nervous system. He has concluded that disorganisatio of bone formation leading to overgrowth is responsible fo compression of the optic nerves and the consequent papil œdema (Mellanby 1938) The results of the present investiga tion suggest that the signs of papillœdema and the compressio of the optic nerves observed by Mellanby may well have bee the consequences of the hydrocephalus which he note (Mellanby 1941) but to which he does not seem to hav attached much importance

The view that abnormal bone growth is responsible for th production of nervous lesions has been accepted by Moor (1930) as the explanation of night-blindness, papillœdem and optic atrophy in calves fed on a diet deficient in vitamin A

Moore et al. (1935) also observed that such calves ha partial paralysis and held their heads in a peculiar position At the same time they considered that the pressure of th cerebrospinal fluid (C.S.F) was raised. Moore and Sykes (1941 reported that there was a progressive increase in the pressur of the C.S.F as the condition developed They observe also that in 1 calf the ventricles were dilated, but apparentl they did not attach any significance to this observation nor do they seem to have reached any definite conclusion about the cause of the increased pressure of the C.S.F Unfortunately in none of these investigations was a detailed histological examination of the brain reported and it i therefore impossible to say whether Moore and Sykes wer dealing with the effects of aqueductal stenosis.

Many other investigators have commented on th incidence of lesions of the nervous system in animal subjected to experimental vitamin A deficiency and i some instances have noted herniations of the brain such as are known to occur in hydrocephalus in man (Wolbach and Bessey 1941) The clinical course of the disease reported in many of these accounts accords closely with the picture observed in the present experiments and

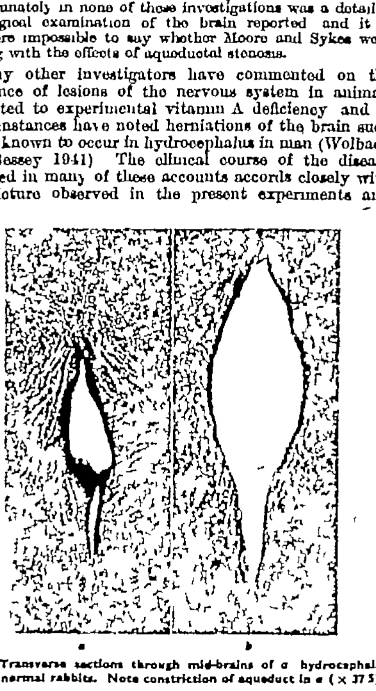

Fig. 3—Transverse sections through mid-brains of *a* hydrocephalic and *b* normal rabbits. Note constriction of aqueduct in *a* (× 37 5)

suggests that the underlying pathology may well have been similar

Hydrocephalus in man has attracted the attention of investigators from ancient times Today most authorities agree that it is often congenital, although the appearance of symptoms may occasionally be delayed until the third or fourth decade The incidence of hydrocephalus due to abnormality of the cerebral aqueduct has been calculated as about 1 in every 9000 births (Woollam and Millen 1953) The authoritative monograph of Dorothy Russell (1949) has clarified the mass of literature on hydrocephalus and has placed its pathology on a sound basis She has classified as the principal maldevelopments of the cerebral aqueduct, stenosis, forking, and septum formation That a deficiency of vitamin A in the mother, and consequently in the newborn, may determine the development of a stenosis of the aqueduct has, however, not hitherto been reported

The clinical picture observed in the present experiments and the histological findings of an obstructive hydrocephalus due to stenosis of the cerebral aqueduct, coupled with the carefully controlled and documented dietary conditions, leave no doubt that there was a causal relationship between the maternal vitamin-A deficiency and the appearance of stenosis of the cerebral aqueduct in the offspring Hydrocephalus and the production of the symptoms of disease of the nervous system followed as a direct consequence of the stenosis

Conclusions and Comment

Although the manner in which the deficiency of vitamin A in the diet of laboratory animals is associated with the production of hydrocephalus by aqueductal stenosis is not yet fully understood, the implications are of great importance The relation of maternal vitamin-A deficiency to hydrocephalus in the offspring opens up a new field of inquiry and merits an extensive clinical investigation

Many important problems concerned with the physiology and pathology of the C S F await solution Surgical interference has been, until now, the only method available for the production of experimental hydrocephalus, and this has been a limiting factor in research into the surgical treatment of the condition The ability to reproduce hydrocephalus in young animals through feeding a diet deficient in vitamin A to the mothers offers a simple and readily available source of hydrocephalic animals for experimental investigations

Many questions remain unanswered and are the subject of further investigation Can hydrocephalus be produced by inadequacy of vitamin-A intake or utilisation after birth ? What is the level of vitamin-A intake necessary to prevent hydrocephalus in the offspring ? Is it possible to arrest hydrocephalus at any stage by supplementing the diet with vitamin A ? Is the aqueductal stenosis a direct result of the deficiency, or is it secondary to some undetermined factor ? At this stage the evidence suggests that the stenosis is the primary condition and the direct result of the deficiency

If the nervous disorders reported in farm animals are equally attributable to stenosis of the cerebral aqueduct, the implications in relation to animal nutrition must be of considerable importance to agricultural economy

Summary

Hydrocephalus occurring in young rabbits as a direct consequence of vitamin A deficiency in the mothers has been investigated.

The underlying cause of this hydrocephalus is stenosis of the cerebral aqueduct

The hydrocephalus has been held to be responsible for the constriction of the optic nerves and for the paralysis found in these animals

These findings are discussed in relation to genetic hydrocephalus and to reports on the effects of vitamin A deficiency on laboratory and farm animals

The discovery of maternal vitamin-A deficiency as a cause of hydrocephalus in the progeny throws open an entirely new field for clinical investigation into the pathology of hydrocephalus, and for experimental observation on the physiology of the cerebrospinal fluid.

We wish to express our gratitude to Prof J D Boyd and Dr J Hammond for their advice and encouragement Thanks are also due to Mr T R L Brooks for the photographs and to Mr R Smith for technical assistance

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AUREOMYCIN-RESISTANT STAPHYLOCOCCAL ENTEROCOLITIS

REPORT OF TWO FATAL CASES

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STAPHYLOCOCCAL resistance to the " broad spectrum " antibiotics is attracting increasing attention (Finland and Haight 1953, Needham and Nichols 1953) Hospitals and other closed communities are recognised to be particularly prolific breeding-grounds for resistant organisms (Lepper et al 1953), the source of increasing numbers of infections for which there is no specific therapy (Spink 1953)

Cases have been published in the U S.A. and in France (Janbon et al 1952, Terplan 1953, *Minnesota Medicine* 1953) in which death took place rapidly and unexpectedly in patients under treatment with aureomycin or with oxytetracycline (terramycin) Diarrhœa, electrolyte imbalance, dehydration, and sometimes a choleriform state have developed suddenly while these antibiotics were being given for infections unrelated to the gastro intestinal canal Many of these patients were in the immediate postoperative period, or had been suffering from the effects of malnutrition or chronic alcoholism.

Coagulase positive staphylococci, resistant to the particular antibiotic in use, were isolated in pure culture from the intestinal canal of most of these patients, before or after death The syndrome has therefore become known as acute, or fulminating, staphylococcal gastro enterocolitis In some cases the staphylococci were shown to belong to enterotoxin-producing strains (Janbon et al 1952), but enterotoxin has not been proved responsible for the condition Indeed, it appears probable that similar symptoms can result from the overgrowth of other antibiotic-resistant organisms normally found in the intestine in small numbers

The two fatal cases described below are believed to be examples of this syndrome

Case-records

Case 1 —A Finnish girl, aged 19, complained on Dec 29, 1952 of pain in the feet, left knee, wrists elbows, and shoulders Next day her temperature was 99°F She gave a history of severe sore throat and a raised temperature four weeks previously when she had stayed in bed a week As a child she had had Ludwig's angina at the age of 6 years and scarlatina at the age of 13 The latter kept her in bed for a ith, and at that time it had been suggested that her heart been affected.

xamination revealed limitation of joint movement owing ain, and an inflamed throat

rse of Illness

reatment with soluble penicillin 0·5 mega-unit six hourly begun. Two days later the patient had severe left infra mmary pain and some signs at the base of the left lung umatic fever had been diagnosed, but therapeutic doses spirin had been without effect. By Jan. 9 1953 hæmolytic ptococci had disappeared from the throat and the penicillin discontinued Pain became worse and was accompanied breathlessness, high fever and exhaustion. Treatment h aureomycin, 0·5 g six hourly followed by 250 mg hourly, was superseded three days later because the ent's condition had deteriorated by oxytetracycline g intravenously and 0·5 g six hourly by mouth Peri ditis and pleurisy persisted. On Jan 11 a widespread rbilliform rash developed which lasted three days.

n Jan. 13 the patient began to have more frequent bowel vements, and two days later frank watery diarrhœa ytetracycline, of which 10 g had been given, was dis tinued, and efforts were concentrated on correcting the ere state of fluid imbalance which had developed but she tinued to go downhill, and she died on the evening of . 19

stigations

During the illness blood-cultures had been repeatedly rile, and no organisms of the enteric salmonella or dysen y groups had been isolated from the stools, which contained merous pus cells. On the patient's admission to hospital up-A hæmolytic streptococci had been isolated from her oat Repeated blood-counts showed a moderate to severe ymorph leucocytosis, with a shift to the left and mild mochromic normocytic anæmia. The erythrocyte-sedi ntation rate remained high throughout the illness. The ne was sterile containing only a few granular and hyaline ts and a few pus cells.

t-mortem Findings

Necropsy on Jan 20 showed a well nourished young girl th occasional bruises on the arms. The œsophagus was rmal. The stomach was distended with gas and some ghtly bloodstained fluid. There were occasional small techial hæmorrhages in the mucosa. The small intestine peared normal containing thin faintly turbid, and bile- ined fluid In the distal part of the colon mainly in the ion of the junction of the splenic flexure and the transverse lon, were some submucosal hæmorrhages and areas of hyper nia, with a few superficial erosions. The colon was distended roughout by turbid bile stained fluid Apart from some bmucosal hæmorrhages the rectum appeared normal In e mesentery were some slightly enlarged lymph nodes (up to 3×1·0×0·8 cm.) which had a pinkish mauve hyperæmic rface on section The liver showed some areas of pale que yellow discoloration, anteriorly and inferiorly extend g for a variable distance into the cut surface It was flabby d contained a moderate to considerable amount of fat. A spicuous fibrinous pericarditis gummed together the ricardial surfaces anteriorly but left enough space to ntain 30 ml of bloodstained fluid, in which were some kes of fibrin. The pale flabby myocardium showed no idence of fibrosis or necrosis. The heart valves, apart from moderate hyperæmia of the aortic valve, were normal There re bilateral bloodstained pleural effusions, with a fibrinous urisy corresponding to the posterior parts of both lower bes and both superior diaphragmatic surfaces. The capsules ripped easily from the mottled yellow red renal surfaces d the moderately enlarged spleen showed only congestion.

Histology.—Microscopy showed no significant abnormality the large intestine There was possibly more loss of structure the part of the mucosa next to the lumen than was likely be due to post-mortem autolysis alone but inflammatory anges were at the most very slight There were small as of degeneration, not acute, throughout the heart muscle ociated with atrophied muscle-fibres, brown pigment, and ne and cellular fibrous tissue There was one Aschoff body the myocardium related to the base of the aortic valve.

Bacteriology.—A profuse growth of coagulase positive phylococci was obtained from the respiratory tract the unum, the descending colon, and the rectum. The staphylo cci were resistant to penicillin, aureomycin, and oxytetra cline but sensitive to streptomycin and chloramphenicol nsitivities were determined by a simple filter paper strip diffusion technique using the Oxford staphylococcus as a control organism.)

The *post-mortem diagnosis* was acute gastroenteritis and acute rheumatism with pericarditis and myocarditis.

Case 2.—A retired college servant aged 65 who had had for more than five years severe and progressive osteo-arthritis of the left hip-joint, and had had a Judet arthroplasty done in November 1951 was readmitted for a revision operation because of persistent pain

Examination revealed that movements in the left hip were almost entirely prevented by pain, and that there was great discomfort both on sitting and on lying down. There was obvious pallor the blood pressure was 180/90 mm. Hg and the heart sounds were faint but normal

The Final Illness

On June 17 1953 the old anterolateral Smith Petersen scar was excised and gross thickening and new bone formation found in approaching the left hip joint The old acrylic head was intact but rather mobile. It was removed the rim of the neck re-reamed and a prosthesis of similar size inserted During the operation the patient received a pint of whole blood

On June 18 treatment with prophylactic aureomycin 250 mg four hourly was begun and next day the patient's condition was entirely satisfactory On June 22 he was rather anxious, complained of pain in the operation site, and had a distended abdomen The bowel sounds were normal Paraldehyde 5 ml was given Frequent bowel movements continued all day and the aureomycin was discontinued

On the following night there was sudden collapse without pain the patient remaining fully conscious. The blood pressure was 90/60 mm. Hg No abnormal signs were found in the heart, lungs, or central nervous system. A blood-count showed moderate normochromic normocytic anæmia. Intravenous fluids and intravenous corticotrophin 25 mg were given. A few hours before death it was considered that a staphylococcal gastro-intestinal infection was the probable cause of his collapse A swab from the rectum, taken at this time subsequently produced a profuse pure growth of coagulase positive staphylococci resistant to penicillin, aureomycin and chloramphenicol but sensitive to streptomycin No organisms of the enteric salmonella or dysentery groups were isolated

In spite of treatment the patient died shortly afterwards

Post-mortem Findings

Necropsy on June 25 showed a well nourished elderly man with a recent surgical scar over the anterior aspect of his left hip-joint. When the peritoneal cavity was opened, moderately dilated hyperæmic loops of small and large intestine presented, whose peritoneal surfaces were smooth and shining No free fluid was present in the peritoneal cavity The whole length of the small intestine cæcum and large intestine contained only small amounts of bile-stained watery fluid The mucosal surface of the small intestine showed slight reddish brown congestion. The mucosa of the large intestine was deeply injected, brownish grey and covered with a loosely adherent incomplete film of fibrinous exudate this appearance being maximal in the cæcum, ascending colon, and transverse colon and absent from the descending colon and rectum The mesentery appeared normal The œsophagus stomach, and duodenum were normal The cut surface of the liver was congested and rather flabby but otherwise normal.

There was slight atheroma of the proximal ends of the coronary and cerebral arteries moderate emphysema of both lungs, and firm fibrous adhesions (up to 3 cm. in diameter) at the base of the left lung and at the apex of the right lung

Histology.—Microscopy showed inflammatory changes in the colon considerably less than had been suggested by the naked-eye appearances. In the transverse colon, which was most affected there was considerable leucocytic infiltration in the base of the mucosa with thrombosed small blood vessels and some (possibly autolytic) lack of nuclear staining in the surface half of the mucosa Throughout the submucosa there was an excess of cells most of which were histiocytes or macrophages with some polymorphs

Bacteriology.—A profuse pure growth of coagulase positive staphylococci was obtained post mortem from the respiratory tract, the stomach the ileum, and the colon. The staphylococci were resistant to penicillin and aureomycin. Coliform bacilli were conspicuously absent.

The *post-mortem diagnosis* was acute staphylococcal enterocolitis following a revision arthroplasty

Discussion

In both cases severe ultimately fatal diarrhœa developed unexpectedly during an illness unrelated to the gastro-intestinal canal, in both cases aureomycin or terramycin had been used to treat the primary disease, and in both cases pure profuse growths of coagulase-positive staphylococci, resistant to the particular antibiotic used, were obtained from the intestine before or after death The gram-negative bacilli characteristic of the normal fæcal flora were conspicuously absent

It seems likely that the use of the broad-spectrum antibiotics led to the elimination of all intestinal bacteria except the resistant staphylococci The latter then grew rapidly and within a few days had selectively colonised the entire intestinal canal. The disturbance in intestinal metabolism thus produced may have been sufficient to cause death in both cases Alternatively the production of enterotoxin by the staphylococci may have been responsible

Both cases are probably examples of a syndrome which has become known as acute staphylococcal enterocolitis

Mild gastro-intestinal disturbances accompanying aureomycin or oxytetracycline therapy are common There is almost invariably some change in the bowel flora (*Minnesota Medicine* 1953) These changes are usually sufficient only to cause mild symptomatic discomfort or inconvenience (Janbon et al 1952) In the patient already weakened by previous disease, however, or after severe operation, the disturbance produced by the alteration in intestinal flora may be sufficiently severe to cause death

The prevention of staphylococcal enterocolitis in hospital patients is made more difficult by the high incidence among the staff of nasal carriers of staphylococci resistant to aureomycin and oxytetracycline and by the large numbers of these organisms present in the ward dust In these circumstances the use of the broad-spectrum antibiotics after major operations, or in particularly debilitated patients, is inevitably accompanied by a certain risk

It has been suggested that this risk of severe enterocolitis could be minimised by careful observation of the fæcal flora during the administration of the broad spectrum antibiotics (Sloss cited by *Minnesota Medicine* 1953) The daily examination of a simple gram-stained film of the fæces would be enough to indicate a radical change from predominantly gram-negative bacilli to predominantly gram-positive cocci.

Should the enterocolitis develop suddenly, and be recognised as a complication of the antibiotic therapy, the only specific treatment for the condition would be to encourage the return of the normal bowel flora This can be done by stopping the antibiotic in use and by substituting a drug to which the staphylococci remain sensitive. Sloss suggested that erythromycin could be used Most staphylococci appear still to be sensitive to this antibiotic, which is known to have little action against the gram negative bacilli (Herrell et al 1953)

Summary

The broad spectrum antibiotics often cause radical changes in the normal flora of the intestinal canal When these changes take place in patients who have recently undergone a serious operation or have some debilitating disease the diarrhœa which follows may be very severe

Two cases are described in which death resulted from the intestinal proliferation of coagulase-positive staphylococci following the administration of antibiotics to which these staphylococci were resistant It is uncertain whether staphylococcal enterotoxin was responsible

This form of staphylococcal enterocolitis may be avoided by daily observation of the predominant fæcal flora Should severe diarrhœa develop, it may be possible to encourage a return of the normal bowel flora by the use of another antibiotic, such as erythromycin, to which the staphylococci are known to be sensitive an does not suppress the gram-negative bacilli.

I wish to thank Dr A M Barrett, university mo anatomist, and Dr M H Gleeson-White, university bac logist, for their advice, and Mr T J Fairbank, or surgeon to Addenbrooke's Hospital, for permission to p his case records.

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AMINO-ACID COMPOSITION OF EIG DERMATOPHYTE FUNGI

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THE amino-acid composition of eight dermatop fungi has been determined qualitatively, by chromatography, using acid hydrolysates of the grown in a simple fluid medium with ammonium sul as the source of nitrogen

METHOD

Microsporum audouini Gruby, *M canis* Bodin, *gypseum* (Bodin) Brumpt, *Trichophyton mentagrop* (Robin) Blanchard var. *gypseum*, *T. discoides* Sabou *T violaceum* Bodin, *T rubrum* (Castellani) Sabou and *Epidermophyton floccosum* (Harz) Langeron Milochevitch were cultured on beerwort agar transplants of aerial mycelium were made into 5 quantities of a liquid medium in conical flasks of 15 capacity The medium was composed of glucose ammonium sulphate 4 g, KH_2PO_4 5 g, K_2HPO_4 magnesium sulphate 0 25 g, ferrous sulphate 1 manganese chloride 1 mg, zinc sulphate 1 mg distilled water 1000 ml, sterilised in an autoclave fungi were allowed to grow at room-temperature occasional agitation by hand. They grew as ma the surface of the medium Only *M. canis* sho distinctive microscopical features under these condi but all the fungi yielded identifiable subcultures beerwort agar

At intervals up to three months the cultures harvested, filtered free from medium, washed distilled water, and dried in an oven at 60°F, with average yield of 300 mg of dry mycelium. The were then hydrolysed with 6*N* HCl for twenty-four ho The hydrolysates were thrice reduced to dryness washed with distilled water The yield was taken in a small volume of distilled water, and samples submitted to two-dimensional partition chromatogra on filter paper, using phenol and 'Collidine' as solv (Dent 1948) *Duplicates* were prepared after treatm of samples of the hydrolysates with hydrogen pero and ammonium molybdate The papers were spra with 'Ninhydrin' to detect the amino acid spots papers were also treated with Pauly's diazo reagent removal of the solvents with acetone

RESULTS

The qualitative results were similar in each Spots corresponding to the expected sites of the follo were seen aspartic acid, glutamic acid, glycine, nine alanine histidine, lysine, arginine, proline, leucine(s) tyrosine cystine (as cysteic acid after tion) [illegible] and methionine (as its sulphone ation) Glucosamine presumably derived from us polysaccharide, was also present No hydroxy ine was detected Tryptophane does not survive hydrolysis baryta and tryptic digests provided tisfactory material for its detection

o great quantitative differences were observed in the position of the eight fungi, judged by the size and nsity of the colours of the spots. The amino acids greatest concentration were the leucines, valine, ine glutamic acid, and aspartic acid These results e at least qualitatively similar to those for various pathogenic fungi (Work and Dewey 1953) including *rospora crassa* *Aspergillus glaucus*, and *Cephalo* *ium acremonium*

DISCUSSION

he fungi producing superficial mycoses grow in the ny layer of the epidermis, the nail plate or the hair t. These structures are composed largely of keratin y also contain non protein substances derived from r parent tissues. Bolliger (1951) for example has onstrated the presence of 3 5% of water soluble stances in clipped rabbit fur Watery extracts of nan hair support the growth of ringworm fungi lsher 1940) but there is little doubt that keratin is r main source of nourishment in parasitic life They e been cultured on pure keratin (MacFadyen 1896) hough no keratolytic enzymes have been found in se fungi (Tate 1929) keratin is undoubtedly broken m. In the case of *M gypseum* the degradation of wool been followed in detail (Stahl et al 1949a and b, 1950) he ability of the dermatophyte fungi to utilise ino-acids has been investigated by various workers g., Robbins (1950) Archibald and Reiss (1950), and mson and Grimm (1951) In such studies the compara e value of various amino acids as sources of nitrogen been examined by adding them singly and in com ation to otherwise complete synthetic media. In eral it has been shown that almost any amino acid l permit the growth of these fungi The sulphur taining amino-acids, so abundant in keratin are nparatively poor sources of nitrogen for the dermato ytes. They do not grow if hydroxyproline is given the sole source of nitrogen. Rothman (1951) has gested that these fungi are obligate parasites of atin because hydroxyproline is absent from the latter

The present study shows that the strains of the eight gi investigated can utilise ammonium sulphate as ir source of nitrogen and that they are autotrophic vitamins. It is not suggested that optimal growth s obtained. The amino acid composition of these gi appears to be similar to that of non pathogenic gi and does not explain the parasitic growth of gworm fungi in keratin. Hydroxyproline was not tected and presumably does not enter into the nitrogen tabolism of these fungi.

SUMMARY

The amino acid composition of eight dermatophyte ngi is qualitatively similar to that of non pathogenic ngi.

No hydroxyproline was detected

I wish to thank Prof. Wilson Smith Dr C. E Work and D Dewey for facilities, guidance and technical aid

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LOCALISED PRETIBIAL MYXŒDEMA
TREATED WITH CORTISONE

R S M D INCH
M B Edin M R C P E
REGISTRAR

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PRETIBIAL myxœdema is usually regarded as a rare complication of, or sequel to hyperthyroidism, but Trotter and Eden (1942) suggested that it may occur in as many as 3% of hyperthyroid cases The first English description was given by Watson Williams in 1895 but since then it seems to have been of greater interest to the dermatologist than to the endocrinologist

Pretibial myxœdema is said to be always bilateral though not necessarily symmetrical and the deposits may not appear simultaneously on both legs and may not develop at the same speed. The histological and biochemical features have been well described by Watson and Pearce (1947) Other workers agree that the connective tissue of the cutis is infiltrated with mucopolysaccharides. The appearance of the skin, with its irregular surface and sparse coarse hair is sufficiently recognised and requires no further description

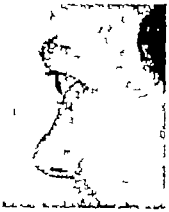
Fig 1 (case 1)—Exophthalmos.

The ætiology of the condition is unknown but is the subject of two hypotheses (1) that the development of the localised myxœdema is the direct result of an unexplained insensitivity of the pretibial tissues to the action of the thyroid hormone and (2) that the lesions, like the exophthalmos with which they are almost always associated are caused in some way by overproduction of the thyrotrophic hormone of the anterior pituitary (Vilanova and Canadell 1949) At present there is little evidence to support either hypothesis.

Various forms of treatment, such as local excision oral and local administration of thyroxine radiant heat, massage and local injections of hyaluronidase have all proved disappointing and Trotter and Eden (1942) concluded that the lesions were not affected by any form of treatment in use at that time

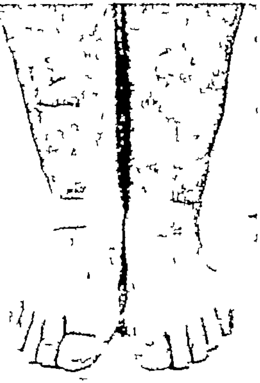
Fig 2 (case 1)—Pretibial myxœdema and deposit on dorsum of right hallux.

We report here three cases which showed some interesting features and describe our experience of the use of cortisone acetate in this condition

Case-reports

Case 1 —A woman developed hyperthyroidism at the age of 36 For the first eight months she was treated with methyl thiouracil, and exophthalmos appeared. As control was unsatisfactory, partial thyroidectomy was performed she subsequently became hypothyroid, and her exophthalmos increased. Coincidently pretibial myxœdema appeared on both legs and her fingers became clubbed About nine months after the operation thyroid treatment relieved the hypothyroidism but had no effect on the pretibial myxœdema Ophthalmoplegia began to complicate the exophthalmos and sixteen months after thyroidectomy her pituitary was irradiated without effect Some three months later she was seen by us for the first time Though her myxœdema was controlled, she had exophthalmos (Hertel exophthalmometer right eye 26 mm., left eye 26 mm.) (fig 1), mild ophthalmoplegia, gross bilateral pretibial myxœdema (fig 2), and marked clubbing of the fingers (fig 3)

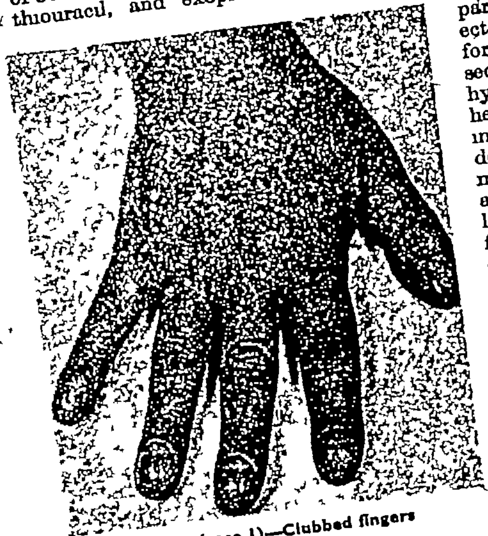

Fig 3 (case 1)—Clubbed fingers

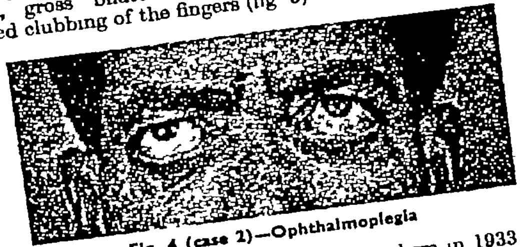

Fig 4 (case 2)—Ophthalmoplegia

Case 2 —A man developed hyperthyroidism in 1933 at the age of 20 and was treated by X irradiation of the thyroid gland He became euthyroid but developed exophthalmos and mild ophthalmoplegia. He remained in full time employment as a miner, but when aged 36 sustained a trivial injury to his left leg and thereafter developed pretibial myxœdema at the site of injury This was soon followed by slight pretibial myxœdema of the other leg A year later the left leg was incised without benefit to the pretibial myxœdema, and a large keloid scar developed at the site of the incision He was first seen by us when he was 39, and although he was euthyroid he had considerable exophthalmos (Hertel exophthalmometer right eye 25 mm , left eye 26 mm.), some ophthalmoplegia (fig 4) and chemosis conjunctivæ The pretibial myxœdema (fig 5) with its keloid scar formed a large mass on the left leg, and there was a smaller area on the right leg, with a pad on the dorsum of the left hallux (fig 6) He also had gross finger clubbing (fig. 7) but did not know when this had started.

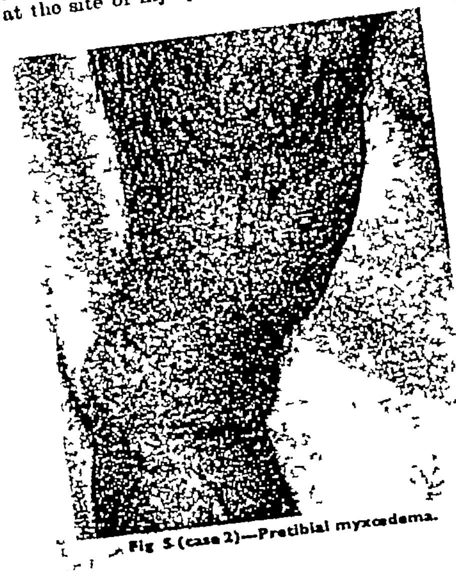

Fig 5 (case 2)—Pretibial myxœdema.

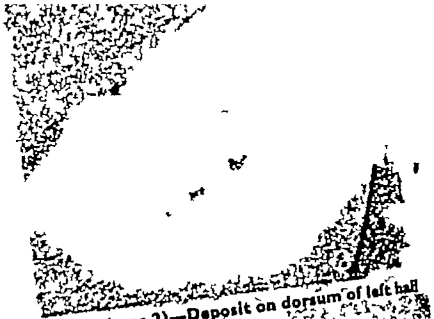

Fig 6 (case 2)—Deposit on dorsum of left hal

Case 3 —A woman had developed myxœdema at the age of 44 and had been treated with thyroid extract She rema well until bilateral exophthalmos appeared at the age of and this was soon complicated by circumorbital œdema ophthalmoplegia, and extensive bilateral pretibial myxœdema When first seen by one of us at the age of 50 she was inade quately controlled with thyroid , and, when the dose of was increased, her ophthalmoplegia disappeared, but exoph thalmos remained, and her pretibial myxœdema was unaffected There was no clubbing of the fingers

This case was exceptional because there was no eviden that the patient had ever had hyperthyroidism.

Treatment

Case 1 was admitted for a trial of the effect of la doses of cortisone in the treatment of exophthalmic ophthalmoplegia (Chandler and Hartfall 1952) She wa given cortisone acetate suspension (Merck) by intramuscular injection After she had had 0 8 g in six days, the plaques of pretibial myxœdema had become softer, especially at their edges, but the exophthalmos was unchanged The systemic administration of cortisone was then supplemented by infiltrating the suspension into an area of pretibial myxœdema An isolated plaque abo 3 cm in diameter was chosen, and 25 mg of cor sone acetate (1 ml of the suspension) was infiltrat with a long fine needle The injection was alm painless, and twenty-four hours later the infiltrated a showed a considerable change compared with untreated part of the plaque The area had shrunk, skin over it had wrinkled and become slightly cyano and the firm thick tissue of the pretibial myxœdema disappeared Two further infiltrations of the same led to the almost complete disappearance of the pla Thereafter the intramuscular injections were di tinued because no improvement was evident in exophthalmos after 1 5 g of cortisone had been adi tered in seventeen days It was, however, thought while to continue the local infiltration of cortisone in

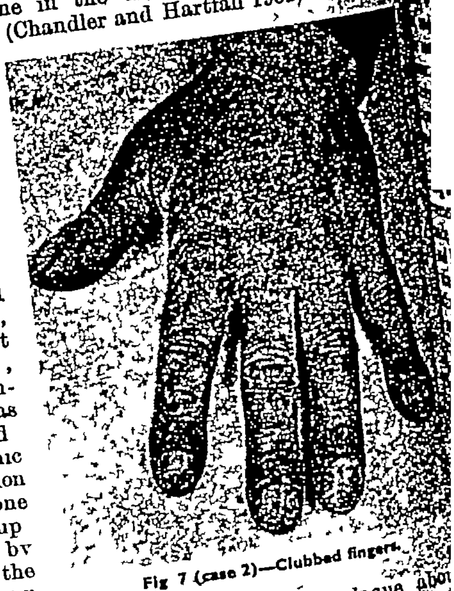

Fig 7 (case 2)—Clubbed fingers.

etibial deposits, and 0·625 g was given in this way in irteen weeks. Although some improvement followed ch infiltration this was less striking than that achieved en cortisone was given systemically in addition to the al infiltration. Hyaluronidase 500 units in 1 ml of ysiological saline solution injected into the pretibial posit so changed its character that within a few minutes became an area of pitting œdema On three subsequent casions a similar dose of hyaluronidase was mixed with ml. of cortisone suspension and infiltrated into the etibial plaque in the hope that the cortisone would ert a more widespread action, but this expectation was t fulfilled The pretibial myxœdema gradually reverted its previous state after the infiltration of any particular ea had been discontinued for some time In view of this e treatment was abandoned

In case 2 intramuscular cortisone was also given for e exophthalmic ophthalmoplegia and 1·0 g was jected in seventeen days without improving the ophthalmos As in case 1 the addition of local filtrations of cortisone given during the period of stemic injections, led to a striking improvement in the etibial myxœdema. When the intramuscular injections ere stopped the local treatment was less successful and versal to the original state took place when the local eatment was abandoned This patient received 0·212 g cortisone by local infiltration in four weeks. Hyaluronidase again failed to increase the effects of the cortisone filtration, and the keloid scar was completely unaffected y the treatment.

Case 3 was not given intramuscular cortisone. In this tient the effects of cortisone infiltration in one leg were mpared with those of hyaluronidase in the other ortisone 0·7 g was infiltrated into the left leg in eleven eeks, and hyaluronidase 9000 units into the right leg the same time In the left leg there was a slight provement after each injection about the same as at induced in the other two patients by the purely local jection of cortisone. In the right leg pitting œdema llowed the injection of hyaluronidase and on two casions the bulk of the plaques was decreased by spirating some of the fluid from the pitting areas The provement, however was transient, and if no aspiration as made the plaque ceased to pit within two or three ys and became indistinguishable from its original state

On the supposition that the pretibial myxœdema and ophthalmos might be different manifestations of the me process, 1 ml of the suspension containing 25 mg f cortisone was injected by Dr G I Scott into the tro-ocular tissues of cases 1 and 2 on the last day of their eatment with systemic cortisone. The only result was a mporary increase in the chemosis, and there was no provement in the proptosis as measured by the ophthalmometer

Conclusions

Intramuscular therapy with large doses of cortisone roduced slight but definite improvement in the pretibial yxœdema of two patients and this improvement was ore striking with the addition of local infiltration of rtisone Local infiltration without any systemic erapy was much less effective in all three cases. We are nable to explain the mechanism by which this combined eatment with cortisone proved beneficial

Although our limited observations suggested that it ight be possible to eradicate pretibial myxœdema by long-continued treatment with systemic and local jections of cortisone, such an attempt was thought njustifiable (1) because of the large amount of cortisone equired, (2) because of the danger of the side-effects of rtisone used in such high dosage and for so long and (3) because of the tendency of the condition to relapse hen treatment was stopped.

The use of hyaluronidase in this condition has already een reported by Rosman (1950) and our studies confirm his opinion that this form of treatment is of no permanent value, further the effect of cortisone is not enhanced by mixing it with hyaluronidase

Although the association of exophthalmos with pretibial myxœdema has often been described, we have not been able to find any reference to gross finger clubbing in such cases Since our interest in this association was aroused by its occurrence in our first two patients we have heard of two other patients in whom the same triad of signs was present The reason for this association is unknown but Coope (1948) mentions that clubbing of the fingers develops occasionally in myxœdema after thyroidectomy

Summary

Three cases of pretibial myxœdema are described In two of them exophthalmic ophthalmoplegia was associated with gross clubbing of the fingers This triad does not seem to have been described before

The effects of treatment with cortisone are described Combined systemic and local injections were followed by definite but temporary improvement in the pretibial myxœdema Local treatment alone was less effective Nevertheless reasons are given why long-continued combined treatment is unjustifiable

Retro-ocular injections of cortisone in two cases failed to improve the exophthalmic ophthalmoplegia

Our thanks are due to Prof D M Dunlop for permission to publish these observations on patients under his care and for his help and advice in the preparation of this paper to Dr G I Scott for undertaking the retro-ocular injections of cortisone to Dr P Hannay for asking us to treat case 2; to Sister E Mutch for her assistance in the treatment of all three cases and to the photomicrography unit of the University of Edinburgh for the photographs

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CORTICOTROPHIN TREATMENT IN POLYNEURITIS WITH PERIARTERITIS NODOSA

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MANY theories have been put forward to explain the acute polyneuritis originally called the Guillain Barré syndrome (Guillain et al. 1916) and now passing under various names such as infective polyneuritis infective neuronitis, and polyradiculitis The view has gained favour recently that it is allergic in origin and a number of workers have therefore treated it with cortisone or corticotrophin (A.C.T.H.) Favourable results have been reported (Newey and Lubin 1953 Blood et al. 1953)

The association of peripheral neuropathy with periarteritis nodosa is well recognised (Kernohan and Woltman 1938 Miller et al. 1949 Summers 1950) the neural disturbance varying from a localised asymmetrical mononeuritis to a diffuse symmetrical polyneuritis Periarteritis is said to respond at times to treatment with corticotrophin and may reasonably be regarded as a manifestation of hypersensitivity Hence it is possible that the associated polyneuritis is also allergic in origin

There are as yet few reports of the use of corticotrophin in the treatment of the Guillain Barré type of polyneuritis occurring with periarteritis The following case is therefore of interest in its therapeutic and ætiological implications.

Case-record

A woman, aged 58, had rheumatic fever in 1910, at the age of 16, with possible involvement of the heart. Subsequently she remained well until 1940, when joint pains and swellings affected mainly the larger joints. These pains recurred intermittently during succeeding years but were never disabling. In July, 1952, however, she developed rather more severe pains and swellings in the knees and hands. She was seen then at the Manchester Royal Infirmary, where examination revealed slight limitation of movements of the hips and knees, swelling of the interphalangeal joints of the hand, and a soft early diastolic murmur down the left border of the sternum. A full blood count was normal, but the erythrocyte sedimentation rate (E.S.R.) was 44 mm. (Wintrobe) in the first hour. Her symptoms were relieved after three weeks' treatment with analgesics and physiotherapy. In February, 1953, an attack of postprandial dyspepsia, to which she had been liable for thirteen years, led to a barium meal examination, which revealed a deformed duodenal cap but no actual ulcer. At this time a blood count showed red cells 4,310,000 per c.mm. and Hb 64%. Medical treatment relieved the dyspepsia, and oral iron therapy increased the Hb to 82% in six weeks. The patient's general health seemed to her to deteriorate, however, and she began to lose weight. On May 15 she developed a severe aching pain across the middle of her back, with an associated numbness of both feet. This numbness spread up the calves within a few hours, and the leg muscles became painful. Next day she felt generally ill, the pain was worse, and the numbness had reached her knees. She was admitted on May 17 to the Manchester Royal Infirmary under the care of Dr. N. Kletts.

On examination the patient appeared ill and in great pain. Her temperature was 98°F and blood pressure 200/100 mm. Hg. A diastolic murmur was heard down the left sternal border. Rheumatoid changes in the hands, effusions into both knees, slight œdema of the ankles, and slight epigastric tenderness were present. The liver was palpable. There were no abnormal motor signs in the central nervous system. The tendon reflexes were absent; plantar reflexes could not be elicited. There was symmetrical loss of all forms of sensation below the knees.

Investigations.—A catheter specimen of urine showed much albumin, some epithelial cells and red cells, but no porphyrins. A blood count showed red cells 4,400,000 per c.mm., Hb 80%, white cells 9200 per c.mm. (polymorphs 70·5%, lymphocytes 25%, monocytes 4%, eosinophils 0·5%). The E.S.R. was 54 mm. in the first hour. Radiographs of the dorsal and lumbar spine were normal. Lumbar puncture produced cerebrospinal fluid (C.S.F.) under a pressure of 120 mm. H_2O, dynamics normal and containing 1 lymphocyte per c.mm., protein 100 mg. per 100 ml., and enough globulin to render it opalescent. The Lange curve was normal. The Wassermann reaction was negative in blood and C.S.F. The blood urea level was 50 mg., the serum albumin 3·3 g., and the serum globulin 3·6 g., per 100 ml., thymol turbidity 5·1 units, and alkaline phosphatase 13·5 King Armstrong units. A pyrocate tolerance test was normal.

Progress.—After two days the back pain eased. The patient's temperature reached 99°F occasionally. Six days after admission she woke to find that she could not move her legs, and that the fingers of both hands were numb. Re-examination revealed complete flaccid paralysis of both legs, in addition to the absent reflexes and the sensory loss previously noted. Calf tenderness was now pronounced. The right posterior tibial artery and the dorsal arteries of the right foot could not be palpated, and the right foot was much cooler than the left. Muscle biopsy (from the left pectoral) revealed no abnormality.

Diagnosis.—Despite the negative biopsy result, the clinical evidence in favour of a diagnosis of periarteritis nodosa seemed overwhelming. The multiple systemic involvement included hypertension, joint changes of rheumatoid type, œdema, albuminuria, anæmia, raised blood urea level, raised E.S.R., evidence of arterial blockage, an enlarged liver with alteration of the serum protein levels, and peripheral neuritis.

Treatment.—In view of the favourable reports of treatment cited above there was a double indication for corticotrophin therapy. On May 20, therefore, five days after the onset of the severe paralysis, treatment with intramuscular corticotrophin gel 20 mg. b.d. was begun. Within twenty-four hours the calf tenderness had disappeared, the patient could move her toes and ankles, and the sensory impairment had receded to the ankles. Absolute constipation, which had resisted treatment for fourteen days, was relieved spontaneously in forty-eight hours. By the sixth day of treatment the patient walked a few steps, and on the tenth day sensory impairment wa limited to the tips of the fingers and toes. At this time she could walk unaided for fifty yards. The effusions disappeared, but the occlusion of the arteries of the right foot persisted. Treatment was discontinued after thirty days, and on July 17 sh was discharged in excellent health.

Re-examination on Nov. 11 showed that her excellent condition was maintained, and by this time all the tendon jerks could be elicited though they were sluggish.

During the course of corticotrophin treatment the patient showed a good eosinophilic response. Certain interesting changes took place in addition to the other accessory clinical findings.

	Days after beginning treatment			
	0	10	21	3
E.S.R.	62	10	13	
C.S.F. protein (mg. per 100 ml.)	100			
Serum albumin (g. per 100 ml.)	3·3	3·1	3·4	4
Serum-globulin (g. per 100 ml.)	3·6	3·5	2·5	2
White-cells per c.mm.	10,800	10,600	9800	89
Polymorphs %	71	84	74	7

The reversion of the serum protein levels to the norma albumin/globulin ratio, the reduction of the E.S.R., an the decrease in the amount of C.S.F. protein follow th clinical improvement very closely indeed.

Discussion

The course of an untreated polyneuritis is rathe variable, which fact makes assessment of treatmen difficult. In the present case, however, the immediat relief of symptoms, which in the previous two weeks ha been developing steadily, coupled with the paralle alteration in certain of the accessory findings, suggests direct benefit attributable to the corticotrophin. Bloo et al. (1953) reported amelioration of severe symptom within four days of beginning treatment in their case, an Newey and Lubin (1953) report demonstrable improvement within thirty minutes of the conclusion of an eight hour intravenous infusion of corticotrophin 25 mg. I is too early to judge the final effect of this form of therap because a relapse may yet occur.

The association of the polyneuritis with a diffus collagen disease—the diagnosis of periarteritis nodosa appears inescapable—raises the question of the pathological process underlying the nerve changes. Lovshi and Kernohan (1949), Miller et al. (1949), Macken et al (1951), and Sahlgren and Hofman-Bang (1950) al describe pathological changes in the vasa nervorum and attribute the neural lesion to ischæmia of the nerve. The symmetrical peripheral distribution of the signs and symptoms is usually attributed to the fact that the longest neurones (running to the periphery) are the most susceptible to the ischæmia. Macken et al. state that th occluded vessels can be recanalised. The explanation o the rapid recovery in the present case may therefore li in the rapid resolution of the subintimal proliferation i the vasa nervorum and immediate relief of the ischæmia. On the other hand, if one regards this symmetrica peripheral neuritis as another manifestation of hypersensitivity, the response to corticotrophin might be attributed to an immediate reversal of biochemical and osmotic changes in the neurones. However, as Mille et al. (1949) point out, perhaps in infective polyneuriti the primary lesion is vascular and not neuronal.

Summary

A case of severe symmetrical polyneuritis with *dissociation albumino-cytologique* of the Guillain Barré type occurring during the course of periarteritis i described. Both conditions responded rapidly to treatment with corticotrophin.

It is suggested that the process underlying this and possibly other forms of polyneuritis is that of tissue hypersensitivity leading either to ischæmia or to more

plex biochemical changes in the neurones These
ges are susceptible of immediate reversal as shown
he rapid response to corticotrophin in the present

are indebted to Dr N Klotts for permission to record
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MOUTH-PIECE FOR USE WITH PNEUMOFLATOR IN RESPIRATORY PARALYSIS

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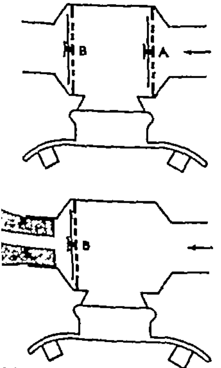
E simple mechanical pneumoflator designed by one s (Beaver 1953) was introduced to provide positive sure respiration during anæsthesia and in cases of re respiratory paralysis due to poliomyelitis For purpose the pneumoflator has been used successfully conjunction with an endotracheal tube or with an sthetic mask of the self sealing type (Goorney 1953) n acute poliomyelitis with bulbar or spinal respiratory ure expert supervision of positive pressure respiration bviously necessary but in chronic or slowly recovering al paralysis the problem is rather different Such ients are best nursed in the conventional box respirator, and the rôle of positive pressure inflation is then to permit severely paralysed patients to be withdrawn from the respirator long enough for nursing attention and physiotherapy to be given efficiently An ingenious positive pressure hood for use with the Both respirator has recently been designed for this purpose (Christie and Esplen 1953)

For these long term respirator cases positive pressure inflation through an anæsthetic mask has the disadvantage that it requires the presence of a doctor or of a specially trained nurse to ensure a good fit of the mask the face and to maintain an adequate ventilating ssure without obstruction of expiration and it is not ways easy to provide adequate supervision for patients quiring positive pressure four or five times a day For is reason a simple non-adjustable mouth piece has been improvised for use with the pneumoflator which makes it possible for assisted respiration to be given safely by the nurses.



1—Standard Siebe Gorman mouth ece above, modified mouthpiece low. For explanation of lettering e text.

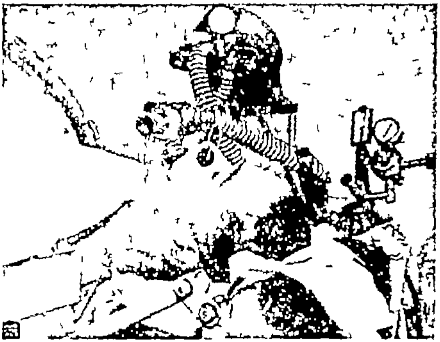


Fig 2—Mouth-piece in use.

The mouth piece (fig 1) is adapted from the standard Siebe Gorman valved mouth piece (catalogue code-word 'Exnick) which is gripped in the patient s teeth, the nose being clipped (fig 2) The inspiratory valve (A) of the mouth piece is removed so that no mechanical barrier exists between the pneumoflator and the mouth but the expiratory valve (B) is retained, and to provide suitable positive pressures during the compression phase a rubber cork (C) bored to leave an air outlet of $^1/_4$ or $^3/_{16}$ inch in diameter is fitted into the outlet Without further adjustment the pneumoflator will then deliver through the mouth piece air or an air/oxygen mixture at a pressure of 10–20 cm of water during compression. No rebreathing takes place and with an outlet bore of the size mentioned there is no appreciable resistance to expiration.

By slight variation in the bore of the outlet hole in the rubber cork, or by the insertion of a short length of glass tubing to reduce its internal diameter the positive pressure produced can be varied between 10 and 20 cm of water without appreciable resistance to expiration and, with a suitable series of corks pressure can be slightly reduced at weekly or monthly intervals according to the degree of recovery of spontaneous respiration.

With this extremely cheap and simple adaptation of a standard piece of equipment positive pressure respiration by pneumoflator becomes a safe routine procedure making it possible to maintain a severely paralysed patient out of a box respirator for long periods without expert supervision At first a patient may be quickly tired by the effort of gripping the mouth piece but within a few days this no longer happens and the patient develops great confidence in the apparatus knowing that if the bite on the mouth piece is maintained no external leak or maladjustment can arise Because the patient is required to grip the mouth piece firmly with his lips and teeth it is only suitable for those with chronic spinal paralysis without bulbar involvement

In one patient with severe spinal paralysis (vital capacity less than 250 c.cm) the pneumoflator and mouth piece have been used four or five times each day for many weeks with a daily total of two or three hours of positive pressure breathing This has allowed a standard of nursing and physiotherapy far in advance of that which could be contemplated if the patient s spontaneous respiration were relied on when out of the box respirator

We particularly wish to thank the many nurses whose coöperation has made routine positive-pressure breathing possible

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Reviews of Books

Approach to General Practice

R J F H PINSENT, M A, M D Camb Edinburgh E & S Livingstone 1953 Pp 166 12s

THIS excellent book answers well to its title In it the intending or actual recruit to general practice will find a clear picture of his future professional life Dr Pinsent is never vague or off the ground He writes as a thoughtful, experienced family doctor, conscious of the duties and opportunities of general practice but not blind to the frustrations and annoyances Established practitioners who read the book will gain an insight into the methods and outlook of a colleague, and specialists a view into what is, unhappily, becoming for many of them *terra incognita*

The chapters on The Surgery, The Doctor's Office, and Treatment in General Practice are full of useful facts and practical suggestions Others, such as those on The Mind of the Doctor, The Education of the Patient, and The Future of General Practice, are more reflective Clear-headedness and reason in all dealings with patients is one of Dr Pinsent's main themes The doctor must not deceive himself by pandering to some patients' woolly conceptions, he must labour to get *their* heads clear too "no placebo under 40 and no tonic at all"

The author is on the whole optimistic about the future of general practice, which he believes will be linked inseparably with that of its College He sees a future for the "general-nursing practitioner" who might "be admitted into junior partnership with the doctor himself"

Surgery of Repair as Applied to Hand Injuries

B K RANK, M S Melb, F R C S, F R A C S, plastic surgeon, Royal Melbourne Hospital, A R WAKEFIELD, M S Melb, F R C S, F R A C S, plastic surgeon, Children's Hospital, Melbourne Edinburgh E & S Livingstone 1953 Pp 256 40s

RECOGNITION of the importance of hand injuries is slowly spreading, and some hospitals now have special departments for dealing with these cases This book will appeal not only to surgeons practising in this special field, but to all general surgeons whose emergency work is sprinkled with hand injuries

The first part describes the social significance of the problem, arrangements for the reception of cases, the special anatomy of the hand, and the clinical examination required The second part deals with primary treatment, which is the most important of all, the third part with intermediate treatment, and the fourth part with secondary treatment The fifth and last part describes the special features of the burnt hand, hand injuries in children, and hand prostheses The whole book is illustrated with good photographs of actual cases

Only a knowledge of plastic surgery can save portions of the hand and fingers which would otherwise be lost, and the section dealing with reconstructive methods applicable to the more severely injured hand is excellent The section on tendon repairs, which are notoriously difficult, is extremely good Mr Rank and Mr Wakefield clearly explain the methods of repair they have found most satisfactory, and their illustrations show the good results that can be obtained

Clinical Endocrinology

LEWIS M HURXTHAL, M D, F A C P, head, department of internal medicine, Lahey Clinic, Boston, NATALIJA MUSULIN, M D, staff of Cooper Hospital, Camden, N J Philadelphia and London J B Lippincott 1953 2 volumes Pp 1600 £9 9s

THE standard work on clinical endocrinology has not yet appeared, nor can it be written until the present phase of rapid advance in this field gives way to a period of consolidation and consideration Meanwhile we are offered on the one hand rather lightweight introductions to what is generally regarded as a difficult subject, and, on the other, unreadable but indispensable works of reference This book falls into the latter category, but the authors have gone one step further than their predecessors they intend this to be a true work of reference and have virtually excluded continuous prose All th material (and it is abundant) is presented in outline forn as a series of lists painstakingly and intelligentl classified, backed by copious references both to early an to recent work, and profusely illustrated This is synopsis rather than a textbook, useless and possibl dangerous to anyone not working in the field, bu invaluable as a labour-saving device to everyone wh practises endocrinology, and particularly to tho engaged in clinical research Here and there tentativ results and rather speculative hypotheses seem to b given equal weight with well-established facts, th references listed must therefore be used with som discrimination

Transactions of the 4th Meeting of the Internation Society of Geographical Pathology

Editors H. H. BETZ and FRED C ROULET Bas and New York S Karger 1953 Pp 396 Sw 46.8

THE *Schweizerische Zeitschrift für allgemeine Patholog und Bakteriologie* have devoted the whole of part 3 o their current volume to a detailed report of the transactions of the 4th meeting of the International Societ of Geographical Pathology held at Liège on July 15-1 1952

The conference was concerned almost exclusively wi infective hepatitis, and included, in addition to individu communications from distinguished investigators, a series o special reports based on the results of a world wide questio ary Among these are a brief summary of the epidemiolog of virus hepatitis, by MacCallum, and a report by Sherlock o the biochemical aspects of acute hepatitis, based on repli received from 22 different countries as far apart as Chile an Japan, Finland, and South Africa. The report contains 4 papers of consistently high standard, and brings together no only the clinical and experimental findings of recent year but much information on related hepatic diseases such a epidemic icterus in French Equatorial Africa, leptospiros and amoebic and parasitic hepatitis The value of th geographical approach to the study of the disease is emphasise by May's outline of the exciting medical programme of th American Geographical Society

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Textbook of Physiology and Biochemistry (2nd ed Edinburgh E & S Livingstone 1953 Pp 1002 50s)— Physiology enters more and more into modern medica thought, and a textbook on the subject, with two profes sors of physiology (Prof George H Bell and Prof. J Norman Davidson) and a distinguished clinician (Prof Harol Scarborough) as its authors, raises high hopes Unfortunatel they are not quite fulfilled in this book, since many section on fascinating subjects have somehow been allowed to mak dull reading Normal phenomena acquire meaning b contrast with the pathological hence the chapters o vitamins and endocrinology are much more alive than mos of the other sections The circus movement theory of auricula fibrillation has been superseded by an account of Prinzmetal' recent work, but unfortunately a good deal of the rest of th book is not as up to date as this. The introductory chapter on biochemistry are more chemical than physiological, an it is difficult to see how the medical student can achieve reasonable synthesis from this disjointed mode of presentatio Needlessly complex accounts are given of matters which coul be expressed as very simple principles A new orientation o teaching in the direction of human physiology is a crying nee in the strenuous curriculum of the medical student toda and this book goes a little way—but only a little way—to mee that need More courage is required to break with the dust past and provide the student with a stimulating and viv account of matters which should become a permanent par of his intellectual equipment But the book is orthodox, an the student who bases his studies upon it will no doubt pa the appropriate examinations.

Supplement to the S.F.A Catalogue of Medical Film (London Harvey & Blythe 1953 Pp 55 6s)—Th *S F A Catalogue of Medical Films* appeared in 1952, bu already some 260 candidates have applied for inclusion Th are well accommodated in this supplement, with the help o which the complete catalogue now gives information on ove 1200 medical films. The supplement should be used with th main catalogue, which contains guidance on the way to us it and a key to abbreviations.

THE LANCET

LONDON SATURDAY DEC 12 1953

Sources of Congenital Heart-disease

DEVELOPMENTS in the surgical treatment of ongenital heart-disease have led to closer study of s *prevalence and causation The true prevalence* unknown, but the observation by McMAHON, lcKEOWN *and* RECORD[1] *that, among nearly two* undred thousand children born in Birmingham etween 1940 and 1949 3 2 per 1000 were affected ggests that it is higher than has been supposed robably even this estimate is too low for it omits atients who lived for more than eleven years without eeding medical attention. Furthermore CAMPBELL nd KAUNTZE[2] now claim a congenital origin for ome cases of aortic stenosis—*a lesion still generally* egarded, at least in young people, as rheumatic heir reasons are chiefly clinical 40 cases, 31 of hich they believed to be valvular because of radiographic evidence of calcification, included 20 with haracteristic signs in infancy or early childhood, hen rheumatism is rare, and a further 17 with uch signs before adolescence In 5 of these patients here was a history of rheumatism, but only in 1 id this precede recognition of a murmur Again, here was no evidence of mitral stenosis in any f these cases nor was the clinical course like that f rheumatic heart-disease Other signs suggesting congenital origin were poststenotic dilatation of the orta soft aortic diastolic murmurs and evidence of ardiac hypertrophy with little enlargement of the eart. Cardiac function was good, but some of he patients died *suddenly At necropsy in such* ases KARSNER and KOLETSKY[3] found inflammatory esions, but CAMPBELL and KAUNTZE suggest that hese may be secondary and should be reassessed n the light of the clinical evidence

Almost all congenital *malformations* of the heart re thought to result from arrested cardiac development in the early months of intra uterine life Even solated defects such as infundibular pulmonary tenosis and subaortic stenosis can be explained n this way and the same explanation probably holds also when the obstruction is at the level of the valves, despite some pathological evidence for the earlier hypothesis of fœtal endocarditis[4] The cause of the developmental failure is not so clear, but both abnormalities of the uterine environment and inherited predisposition are known to be important. The classical observations of GREGG,[5] who found 44 cases of congenital heart-disease of one kind or another in 78 children with congenital cataract following maternal rubella in early pregnancy, have been amply confirmed SWAN et al.[6] found 21 cases among the children of 01 mothers who had had rubella in the first three months of pregnancy, and similar observations *have since been described repeatedly*[7] There is nothing to suggest that other virus infections, such as measles and poliomyelitis have the same effect, possibly the reason is that these kill the fœtus Patency of the ductus arteriosus seems to be associated with fœtal distress at birth suggesting that prolonged anoxia may play a part in its causation The children of women who have had repeated still births or miscarriages seem to be rather more apt than others to have a congenital disorder of the heart Inherited characteristics are always difficult to prove unless they behave as dominants or produce common *or benign lesions* The *association of heart-disease* with other inherited defects, including mongolism and arachnodactyly is well known and sometimes more than one member of a family has a congenital cardiac lesion COURTER et al[8] found reports of *03 families in which more than one member had* any of several types of lesion but particularly atrial septal defect CAMPBELL[9] found that of 110 consecutive patients 7 had affected siblings—more than would be expected by chance In Birmingham McKEOWN *et al*[10] *investigated the families of 431* cases drawn from 425 fraternities, and found 6 affected among 342 siblings born after the propositus this is a proportion of 18 per 1000 which is considerably greater than that in the general population They could *not estimate the likelihood of siblings having* similar lesions, but on the whole thought that they tended to do so The proportion of affected parents was probably no greater than that in the adult population Two first-cousin marriages each produced a child with dextrocardia (*thus supporting* COCKAYNE's[11] view that visceral transposition is due to an inherited recessive gene), while one second cousin marriage produced a child with œsophageal atresia and cor biloculare

This rather *incomplete* picture would perhaps be made clearer by a study of twins but there can be little doubt of the importance of genetic as well as of environmental factors The prognosis for patients with congenital heart-disease is bad in the Birmingham *series, of every 10 affected children only 3 reached* the age of ten years Surgery has improved the chances of these patients, but even so the outlook is gloomy enough to make us want to know more about causation

Antibiotic Enterocolitis

IN *this issue Dr* GARDNER *reports two cases in* which severe and ultimately fatal enteritis unexpectedly and suddenly developed during the administration of aureomycin or oxytetracycline (terramycin) to patients whose primary illness was unrelated to the gastro *intestinal* canal. In both cases pure and abundant growths of antibiotic resistant coagulase positive staphylococci developed in cultures from the intestinal and respiratory tracts the gram negative bacilli characteristic of the normal fæcal flora were conspicuously absent In the U.S.A. and France

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similar cases have been reported,[1–4] and clearly we must examine the facts surrounding this dangerous complication of antibiotic therapy

Oxytetracycline and aureomycin are the antibiotics especially implicated, but FAIRLIE and KENDALL[2] observed the same type of enteritis in patients given a combined course of penicillin and dihydrostreptomycin by intramuscular injection. Obviously there is need for discretion in the choice of antibiotic, to prevent postoperative infection or to treat an established infection, where the patient's general condition is much reduced either by severe or long-continued infection or by such states as malnutrition and chronic alcoholism For example, weighing risk against likely gain, the powerful bactericidal effect of streptomycin and penicillin is essential for the successful treatment of endocarditis caused by *Streptococcus fæcalis*, since the infection is not otherwise curable the hazard of this particularly powerful combination is justified But it is doubtful whether such a combination can justifiably be given to prevent postoperative infection The "broad-spectrum" antibiotics—aureomycin, oxytetracycline, and chloramphenicol—have obvious attractions as prophylactics in that they are given by mouth and protect against so many organisms, particularly those of the intestinal tract But these drugs rather often provoke some gastro-intestinal disturbance, and it is a mistake to suppose that the symptoms are always either mild or transient At the recent Washington symposium on antibiotics[5] the discovery of a new antibiotic, tetracycline ('Achromycin'), was announced The chief advantage claimed for it is that it causes much less nausea, vomiting, and diarrhœa than either of its near relatives, aureomycin (chlortetracycline) or oxytetracycline, with which it shares many properties If this is confirmed the new drug will indeed be welcome Meanwhile in choosing prophylactics it should not be forgotten that succinylsulphathiazole by mouth and penicillin by injection provide good cover with little risk, and that moderate dosage over a short period is likely to be effective Altogether it seems that much current practice is based on unduly pessimistic estimates of the risk of sepsis complicating operations, with the result that patients are being needlessly exposed to real dangers by over-insurance against complications which are improbable and which can readily be controlled by prompt treatment with antibiotics There can be no substitutes for a sound aseptic technique and for watchful care during convalescence, these will contribute far more to the safety and welfare of patients than a carefree enthusiasm for hearty doses of the latest antibiotic Before the era of sulphonamides and antibiotics sepsis had become a relatively rare complication of deliberate operations

We normally live on peaceful terms with our intestinal bacteria, and it seems almost ungracious and certainly naïve to disturb their balance suddenly in preparing for a surgical operation We cannot by giving known antibiotics eliminate all forms of living micro organism from the intestinal tract, and we must expect that suppression of the species sensitive to the chosen antibiotic will favour proliferation of those which are insensitive We still know little of the complicated influences governing the ecology of the bacterial population of the intestine, but common sense suggests that it may be best for the patient to weather a surgical crisis in company with the organisms with which he has come to terms Perhaps staphylococci are not the sole cause of the enterocolitis reported by Dr GARDNER and others, but many coagulase-positive staphylococci produce enterotoxin and may give rise to sharp outbreaks of food poisoning. Owing to our own activities, staphylococci in hospitals are now largely resistant to the antibiotics in general use, and it has been suggested that erythromycin, as it becomes available here, might be reserved for cases of staphylococcal enteritis Such restraint, however, would not be in keeping with the general popularity of new antibiotics, and in any event erythromycin resistant staphylococci appear very readily In the Washington symposium,[5] LEPPER referred to a hospital in which after five months' use of erythromycin the carrier-rate of highly resistant strains reached 75% The remedy seems to involve, firstly, educating ourselves to use antibiotics sparingly, taking full advantage of other means of preventing surgical sepsis, and, secondly, undertaking careful and critical studies of the normal intestinal bacteria and of the influences, including antibiotics, which determine important changes in this richly varied population

Peripheral Neuropathies

FEW nosological problems can be more difficult than that of the peripheral neuropathies Rational classification is difficult because of the wide clinical variations and the complex pathological and biochemical findings[6] Accordingly in treatment the tendency has been to apply any remedy for which success has been claimed, regardless of the type of neural disorder

Clinically the disturbance may be peripheral, in the nerve roots, in the spinal cord, in the brain, or in the cranial nerves, but this variation only suggests varying susceptibility of the neuronal groups Pathologically, too, the findings vary enormously For instance, in the Guillain-Barré syndrome (infective neuronitis, infective polyneuritis, polyradiculoneuritis), SCHEINKER[7] was impressed by the pronounced swelling of nerve-fibres in the spinal roots and cord tracts and in the cranial and peripheral nerves, while LOWENBERG and FOSTER[8] described degeneration of the myelin in the peripheral nerves, spinal cord, ganglia, and brain stem FORSTER et al,[9] on the other hand, found that the central nervous system was not materially affected Such different pathological findings clearly reflect the differences in the clinical picture, they are no doubt due partly to differences in the temporal evolution of the disorder Biochemically a few features are now clearly defined JOINER et al[10] showed that neuropathy due to

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[1] *Minn. Med* 1953, 36 63

[2] Fairlie C W Kendall, R E *J Amer med. Ass* 1953 153 90

[3] Terplan K *Amer J Path* 1953 29 595

[4] Janbon, L. Bertrand J Roux J, Salvaing J *Bull. Acad Med., Paris* 1952 136 59

[5] See *Brit Med J* Nov 7 1953 p 1013

[6] See Elkington J H C Thompson, R. H S Matthews, W B *Proc R Soc Med* 1952, 45, 661

[7] Scheinker L M *J Neuropath* 1949 8 184

[8] Lowenberg, K Foster, D B *Arch Neurol. Psychiat., Chicago* 1945 53, 185

[9] Forster F M. Brown M, Merritt H. H *New Engl. J Med* 1941, 225 51

[10] Joiner C L McArdle, B Thompson, R. H S *Brain*, 1950, 73 431

in B_1 deficiency is associated with inhibition of yruvate-oxidase enzyme system, and THOMPSON[10] pointed out that abnormally high blood pyruvate s may be found not only in patients with neuro y associated with vitamin B_1 deficiency but also hose with toxic neuropathies due to lewisite, ic or other metals These substances are believed sturb the pyruvate-oxidase system by their attrac for the sulphhydryl groups of the enzyme elns. In the deficiency neuropathies (possibly iding some diabetic forms) it is reasonable to uister vitamin B_1 and in the toxic neuropathies ercaprol (BAL) which is believed to restore enzyme librium In the majority of neuropathies however e is no clear indication that either vitamin B_1 iency or intoxication is at work—and this seems apply also to the rare neurological affections ciated with porphyria and with carcinoma

he most common form is the Guillain Barré lrome, and it is chiefly in this group that the ous remedies have been assessed VAN HAGEN BAKER[11] have described their experiences in cases treated with a combination of vitamin B_1 dimercaprol They found that about half of e patients seemed to ' show improvement " and cluded that this improvement indicated that the drome was itself due to disturbance of the enzyme system Other workers have suggested an allergic basis emphasising the histological picture of œdema of the neural tissues leading to secondary myelin degeneration These days such a hypothesis leads inevitably to a trial of cortisone or corticotrophin (A C T H) Among others, BLOOD et al[12] and NEWEY and LUBIN[13] have reported dramatic improvement in the Guillain Barré syndrome after administration of 25 mg of corticotrophin intravenously over a period of 8 hours each day for 5–10 days Discontinuation of treatment was followed by relapse, but this was successfully countered by a further course In this issue Dr LIVERSEDGE and Dr LEATHER report a good response in a patient with polyneuritis associated with periarteritis nodosa This association is well recognised, and it seems possible that both disorders may be due to tissue hypersensitivity which may be primarily neuronal or due to affection of the vasa nervorum Apparently allergy may play an important part in the Guillain Barré syndrome, the sensitising agent is still unknown but this syndrome almost invariably follows some minor infection Furthermore the polyneuritis associated with measles mumps, diphtheria, and even porphyria might also be explained by this hypothesis. Though the evidence is still imperfect, the day may be approaching when neuropathies can be treated more rationally

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Van Hagen, K. O Baker R. N J Amer med. Ass. 1953 151 1163

12 Blood A., Locke W., Carabasi R. *Ibid*, 1953 152 139

13. Newey J A. Lubin R. L. *Ibid* p 137

Annotations

CLINICAL RESEARCH BOARD

HE Medical Research Council announces this week membership of the Clinical Research Board, set up ccordance with the white-paper on Clinical Research Relation to the National Health Service[1] The board ointed for three years after consultation with the istry of Health and the Department of Health for tland has the following members

ir GEOFFREY JEFFERSON F.R.S. emeritus professor of rosurgery University of Manchester (chairman); Prof GALD BAIRD midwifery department University of Aber n; Sir HENRY COHEN department of medicine University Liverpool Prof E. C DODDS F.R.S., Courtauld Institute Biochemistry Middlesex Hospital London Sir JAMES ARMONTH, department of surgery University of Edinburgh f. A. J LEWIS Institute of Psychiatry Maudsley Hospital, ndon; Prof G W PICKERING medical unit, St. Mary's spital, London; Prof R. PLATT department of medicine, iversity of Manchester; Sir JAMES PATERSON ROSS, gical unit, St Bartholomew's Hospital, London Sir MES SPENCE, department of child health King's College wcastle upon Tyne and Prof. B W WINDEYER, Meyer in Institute of Radiotherapy Middlesex Hospital London. e chief medical officers of the Ministry of Health the partment of Health for Scotland and the Ministry of alth and Local Government in Northern Ireland will be essors to the board and the secretary of the Medical search Council will attend all meetings. Dr F J C erald, a senior medical officer on the council's headquarters aff will act as secretary

The board will be concerned with promoting whatever inical research needs to be organised on a national basis. t will aim to ensure that all fields of inquiry are ade ately covered, and will collect, collate, and distribute formation in order to reduce the time-lag between iscoveries and their application

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[1] See *Lancet* July 18 1953 pp 123 133

TEETHING-POWDERS

AT an inquest last week the death of a child aged ten months was attributed to bronchopneumonia due to pink disease, itself the result of mercury poisoning following innocent overdosage of teething powder[1] Last year the Minister of Health, replying to a question in the House of Commons said that the indiscriminate use of teething powders containing mercury is clearly undesirable [2] This advice has been unheeded and teething powders containing calomel are still being sold to the public without adequate warning about their dangers.

In his article[3] last week Dr Farquhar described two more cases where mercury caused or contributed to death one child died from severe renal damage, apparently a similar condition to that reported by Wilson et al.[4] and the second showed many of the clinical features of pink disease The nephrotoxic action of mercury is undisputed and these reports alone are sufficient to proscribe the use of mercurials in infancy But the rôle of mercury in pink disease is not yet clearly defined: that the disease is a form of poisoning by or hypersensitivity to mercury has been strongly suggested by the work of Fanconi[5] in Switzerland and Warkany[6] in the U S.A They have shown that in many cases of pink disease there is either a history of mercury ingestion or inunction or an excretion of excessive amounts of mercury in the urine This is true also of reports from this country[7, 8] Australia[9] and South Africa.[10] These have demonstrated the interesting correlation between

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1 *Times*, Dec. 3 1953
2 See *Lancet* 1952 i, 827
3 Farquhar H. G *Ibid* Dec. 5 1953 p 1186
4 Wilson, V K. Thomson M. L. Holzel, A. *Brit. med. J* 1952 i, 358.
5 Fanconi, G., Botsztejn A. *Helv paediat. acta* 1948 3 264
6 Warkany J Hubbard D M, *J Pediat* 1953 42 365
7 Holzel A., James, T *Lancet* 1952 i, 441
8 James, G V. *Gt Ormond St J* 1951 i, 48
9 Clements, F W *Med. J Aust.* 1953, ii, 213
10 Epstein, B *S. Afr med. J* 1953 27 3*3.

the age distribution of the disease in various parts of the world and the differing mercury habits of the population. Fanconi has produced positive skin reactions to mercurials in affected children, while Warkany has drawn attention to the symptoms shared by pink disease and mercury poisoning. The beneficial effect of dimercaprol (B.A.L.) in some cases of pink disease also points to mercury as a possible cause.

On the other hand, many pædiatricians are unconvinced that mercury is a common cause of pink disease in this country, for various reasons. Often there is no history of mercury having been taken, and, when there is it is likely that it has been given as "home treatment" in the early stages of already established pink disease. Oliguria with a concentrated urine is typical of pink disease, so the finding of an excess of mercury in single specimens is not conclusive proof of an abnormal daily output. Fewer infants are now ritually purged with calomel, but pink disease is rather more common. Holzel and James[7] found more cases in an area where only 7% of infants regularly received teething-powders than in a neighbouring county where 37% had regular doses. As Pehu[11] demonstrated, pink disease tends to occur in epidemics, but it is doubtful whether the administration of mercury shows similar fluctuations. The natural history of pink disease is unlike adult mercurialism, nor does it accord with recognised hypersensitivity reactions. Finally, James[8] found that treatment of the mouth lesions with mercurochrome did not adversely affect the course of the disease. In spite of these potent criticisms, it is likely that mercury plays some part in some cases of pink disease—and there is certainly as yet no other very satisfying explanation of the condition. Recent alternative hypotheses, such as the endocrine approach of Cheek[12] and the psychosomatic basis of Leys and Cameron,[13] are not entirely convincing, so the student of pink disease may say, with Lady Blanche, "there's an unbounded field of speculation, on which I might discourse for hours."

Whatever the final conclusions may be, there is an immediate practical issue. Seven million teething-powders of the most popular brand are sold annually, some of them on medical advice. Each contains half a grain of calomel, which has no therapeutic properties superior to those of relatively harmless drugs. It is surely time that calomel was withdrawn from the formulæ of teething-powders.

NOCTURNAL MYOCLONUS

MANY people have occasionally experienced the sudden start which may momentarily wake them just as they are dropping off to sleep. Jack London had a pleasing phylogenetic explanation for it in one of his novels. He suggested it was the vestigial remnant of the protective start which roused man's arboreal ancestors as they were about to fall from their sleeping perch to the dangers below. In some people these nocturnal jerks may be frequent and repeated, and for these cases Symonds[14] proposes the term nocturnal myoclonus and suggests that this is an epileptic variant. Of 5 cases which he describes in detail, there is suggestive evidence in 2 of other epileptic manifestations, while in 2 others the setting of attacks or their precipitation is reminiscent of the type of reflex myoclonic epilepsy well known to neurologists.

The mechanism of the generalised reflex myoclonic jerk is of considerable physiological interest. It must represent the sudden momentary discharge of some centre having access to widespread motor pathways, and is peculiar amongst epileptic phenomena in showing no change in consciousness and ending abruptly almost as soon as it begins. This latter feature may suggest an active inhibitory element, such as is seen so prominently in the cataplectic attack, itself sometimes precipitated by sudden surprise. Neurophysiologists are now familiar with subcortical centres, such as the mid-brain reticular formation, which mediate widespread motor inhibition or discharge. It may be that nocturnal myoclonus represents an abnormal discharge from such lower levels where functional representation is less differentiated and where inhibition and excitation are more closely juxtaposed. But the evidence for regarding *all* such cases as basically epileptic does not at present seem very great. It is perhaps still a matter of clinical impression; which, when properly interpreted, can supply the hypothesis which adds value to further observations.

RENAL TRANSPLANTATION

THE transfer of tissue to a new site in the same animal or patient is described as autotransplantation; the transfer of tissue from one subject to another of the same species as homotransplantation. Autotransplantation of skin and bone is an established part of surgical practice; and homotransplants of bone, artery, and cornea have been successful in many patients. There is doubt, however, as to how far homotransplants of bone and artery are actually viable; they may merely form an appropriate scaffolding for new tissue growth. Corneal grafts are in rather a special category, since they contain very few cells and are relatively or completely avascular; and this reduces the likelihood of the immunity responses which destroy the generality of homografts.[1] Rather different problems will have to be solved before homotransplantation of complex organs, such as the kidney, becomes practicable; but increasing skill in vascular anastomosis, and increasing knowledge of the structure of immunity in different individuals of the same species, allow us to hope that these will be solved. Meanwhile, bold attempts are occasionally made to anticipate the future.

In December of last year, a boy of 16 fell from a scaffolding and ruptured his right kidney; after this had been removed at an emergency operation it was found that his left kidney was hypoplastic, and not forming urine. When he had been anuric for a week, his mother insisted that one of her kidneys should be grafted into the patient; and this was done, the kidney being ischæmic for only 55 minutes. Urine formation began at once, and in a few days red cells and protein disappeared from the urine. The blood urea fell from over 400 mg. to less than 100 mg. per 100 ml.; and the urea clearance of the grafted kidney ranged between 8.4 and 14.2 ml. per min. The urine volume was over 3 litres when the blood urea was high, and at this time there was considerable electrolyte loss in the urine; later, the urine volume fell with the blood-urea, although the urea clearance remained constant—findings of great interest in relation to Platt's hypothesis that the polyuria of renal failure is largely an osmotic diuresis.[2] After 16 days the patient was allowed up, and some protein appeared once again in the urine; on the 21st day after grafting the flow of urine stopped abruptly, and the kidney swelled to twice its size; and the patient died after a further period of anuria. At necropsy the kidney showed cellular damage in both glomeruli and tubules; there was also vascular damage, with hyaline necrosis; but the blood pressure had been raised for some time before death, and the vascular changes may have been related to this, and not to the renal "apoplexy" which happened so suddenly on the 21st day after grafting.

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[11] Pehu, M., Ardisson, P. *Bull. Soc. Pédiat. Paris,* 1926, 24, 152.
[12] Cheek, D. B. *J. Pediat.* 1953, 42, 239.
[13] Leys, D., Cameron, K. *Brit. med. J.* 1952, i, 191.
[14] Symonds, C. P. *J. Neurol. Psychiat.* 1953, 16, 166.

[1] Maumenee, A. E. *Transplantation Bull.* 1953, 1, 7.
[2] Platt, R. *Lancet,* 1951, i, 1239.

here was a progressive rise in the gamma-globulin action of the patient's plasma proteins this supports e suggestion that the renal catastrophe was due to rmation of antibodies to the foreign kidney but there as no deviation of complement

Reporting this case Michon et al.[3] point out that the dney perished despite the satisfactory vascular anasto oses the absence of infection and the close relationship f donor and recipient. They attribute the destruction f the kidney to an immune reaction, pointing out that e time taken for this to develop is comparable to that und in homotransplantation experiments from the oneer work of Carrel[4] onwards. Their observations o show however, that a grafted kidney can function efully, though not normally—a limitation which pplies even to autotransplanted kidneys in dogs[5]

Attempts have also been made to transplant kidneys to patients with chronic nephritis[6] Almost all have iled sooner or later, commonly because of infection voured perhaps by the use of cortisone or corticotrophin, ven with the object of suppressing immunity mech nisms. Some hope, however, is to be had from Miller's[7] port of the survival of one transplanted kidney for ½ months, after which the patient died because f his persistent hypertension and not because of renal ilure, the blood urea having fallen to 33 mg per 100 ml t present it seems that a renal homotransplant is most but not absolutely certain to be destroyed herein lies the stimulus to further effort, and perhaps r the moment this should be experimental rather than inical, lest vain hopes be raised

CORTICOTROPHIN AND CORTISONE IN DERMATOLOGY

The Ministry of Health recently announced[8] that pplies of corticotrophin (A.C.T.H.) and cortisone are to e made available for the treatment of a limited number f diseases, including certain dermatoses Up to now pplies of these hormones for dermatological use ave largely been distributed by the Medical Research ouncil. The report of the panel of dermatologists o whom their use was entrusted has not yet been ablished.

In a summary of four and a half years experience 'Leary and Erickson[9] describe two main categories of kin disease in which they consider the use of cortico rophin and cortisone indicated. One group comprises therwise fatal disorders, notably pemphigus vulgaris and stemic lupus erythematosus here treatment may have o be sustained for years, although there may be periods f remission when it may be temporarily suspended On the other hand, in self limited but violent skin reactions uch as severe contact sensitisation dermatitis or acute drug eruptions a few days treatment with the hormones may suffice. O Leary and Erickson stress that the great majority of patients with skin disorders do not benefit from this treatment. The usual general contra-indications for their use apply equally to skin diseases, and, in addition acrosclerosis is a special risk, 6 patients with this disorder died of "cerebrovascular accident associated with severe hypertension and renal disease after treatment with cortisone. The success of treatment may be limited by irreversible damage for example in lupus erythematosus the impairment of cardiovascular and renal function imposes particular difficulties in the use of these hormones and convulsive seizures may be increased in frequency[10] and necessitate interruption of treatment.

When long-continued use of corticotrophin or cortisone is necessary, it is often difficult to devise a dosage which will control the disease without producing serious side-effects This danger cannot be overcome by the local application of cortisone which is of no value when used in this way There is some hope that Compound F may be effective by local inunction[11] it does not seem to cause systemic effects judging by the number of circulating eosinophils when given locally[12]

Corticotrophin and cortisone are not curative in any skin disease in the sense that they abolish the underlying pathological process. They appear to modify the body's reaction to the process but unless the cause is removed the disease continues as it were 'underground.' Thus, in systemic lupus erythematosus, the laboratory can detect signs of activity although the patient is relieved of symptoms In epidermal sensitisation, eczema may be suppressed but patch testing shows that the hyper sensitivity persists Moreover, not all cases respond and they may in fact grow worse during or after stopping treatment It is therefore obvious that useful as these substances may be in the suppression of symptoms, they are by no means the answer to the dermatologist's prayer

THE MOTHER AND THE NURSERY SCHOOL

The idea that civilisation begins in the nursery is not new but the corollary—that the mother as prime civiliser needs every tool in the way of intelligence education and skilled help that Nature and the Treasury can afford her—is as yet only dimly apprehended. She can however get skilled help of a particular kind from the nursery school The W H O Unesco advisers on mental hygiene in the nursery school, who met in Paris in 1951 and whose report[13] has now appeared, are careful to draw a distinction between the nursery school proper, which provides for a few hours daily, an extension and enrichment of those opportunities for development which the child in his early years gets in his own home, and the day nursery which has to provide substitute maternal care throughout the day for infants and young children whose mothers are out at work or for other reasons unable to look after them. It is true that many day nurseries provide some preschool education on nursery school lines but this is usually a secondary function. The child attending a true nursery school spends most of his time with his mother the child in the day nursery may spend as much as 12 hours of the 24 away from her The day nursery then ought to be planned to give him as good a substitute for maternal care as possible and also to offer him the chances provided by the nursery school The same staff, the group say, cannot be responsible for both those who give care throughout the day should be relieved, during a part of the day by those who give him preschool education

The years between infancy and school life are packed with emotional experience During them the child is normally building up a concept of his self separate from reality (as he conceives reality) but having a relationship with it. He also develops a personal relationship with another person—his mother—and through this experience learns to form a personal relationship with someone other than his mother This person is often the nursery-school teacher and through her he will develop the capacity to form relationships with several people, including those of his own age She must therefore be a person of special qualities, and carefully prepared for her

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3. Michon L., Hamburger J., Oeconomos, N Delinotte P., Richet, G., Vaysse J Antoine B *Pr med.* 1953 61 1419
4. Carrel, A. *J exp. Med.* 1908 10 97
5. Dempster W J., Jockes, A. M. *Acta med scand* 1953 147 93
6. Hume D M., Merrill, J P., Miller B F *J clin. Invest* 1952 31 610.
7. Miller B F *Transplantation Bull.* 1953 1 17
8. *The Lancet,* Aug. 29 1953 p. 450
9. O'Leary P A., Erickson, J G *J Amer med. Ass.* 1953 152, 104.
10. Mitchell Heggs, G B *In* Cortisone and A C.T.H Edited by W S. C. Copeman London, 1953
11. Sulzberger M. B Witten, V H. Smith C. C. *J Amer med Ass* 1953 151 468
12. Smith, C. C *Arch Derm. Syph., N Y* 1953 68 50
13. Mental Hygiene in the Nursery School. Unesco. H.M. Stationery Office 1953. Pp 33 1s.

job someone at ease with herself, with warmth, kindness, and objectivity—not someone who has taken up the work to satisfy her own emotional needs

Methods of training for this work differ in different countries, here it is usual for girls leaving school to enter as nursery school student nurses, some go on to become heads of nursery schools while others use this experience as a preparation for a nursing training In some other countries, however, the candidate trains as a teacher, and only decides towards the end of her course in what kind of school she wants to teach She thus has the advice of her teachers in making her choice, and if the choice turns out to be a wrong one she can change to some other branch of teaching, since her qualification is valid in any kind of primary school

A successful nursery-school career, the group say, depends primarily on "the teacher's own understanding of children, developed through a continuous experience with them during her own period of growth" Unfortunately this experience is not as common as it used to be, and "many growing girls are unprepared for the emotional responsibilities of motherhood" The reformers of the last century who prised open the gates of education for girls were obliged to direct them along the road trodden by boys that way only lay equality of academic opportunity An unforeseen result of this has been that the ancient and respectable career of childbearing and child rearing has acquired an amateurish aspect no diplomas are given, and the training—now that families are small—is deplorable "Only too often," the group say, "the young mother's first baby is also her first intimate contact with a preschool child", and they do not suppose that domestic science and motherhood classes for school-leavers can fill the bill "Rather our educational system should make it possible for older girls naturally to take small responsibilities for younger children, and particularly for children of preschool age" The prime civiliser, in fact, should be given early and adequate experience of the sort of people she will have to civilise

RADIOGRAPHY OF THE MAXILLARY ANTRUM

IN 1891—the year after Rontgen discovered X rays—Scheier[1] reported on the value of radiography in the diagnosis of diseases of the nose and throat, but the quality of his films was poor and the outlines of the sinuses could hardly be seen Nowadays, however, technique is so nearly perfect that radiography is without doubt the most useful adjunct to the clinical diagnosis of antral disease

Burtoff[2] found that the radiological reports of maxillary sinusitis were confirmed by proof puncture or other operation in 86 out of 100 cases Ballantyne[3] correlated proof puncture findings with X ray appearances in a series of 75 cases of suspected antral infection Of 66 cases in which there were radiographic changes 57 showed evidence of infection on lavage Perhaps even more encouraging is the fact that in the 9 cases where there was no radiographic abnormality, the washings showed no evidence of infection This is important, for the same cannot be said of other methods such as transillumination, which may indicate that an antrum containing pus is completely clear In a further series of 206 cases Ballantyne and Rowe[4] confirmed the earlier findings Three main groups were distinguished the first group consisted of 10 cases in which the antra were completely clear on radiography, the second contained 88 cases in which the antra were completely opaque, and the third consisted of 82 cases with radiographic appearances of a thickened membrane On puncture, there was no naked eye evidence of infection in any of the cases that were radiographically clear, more than 8 out of every 10 that were opaque in the film gave positive findings on lavage, while in less than 1 in 10 of those with a "thickened membrane" pus or mucopus was found in the wash out It would thus seem that a negative radiograph of the antrum is pretty reliable

What causes radiographic changes in the antrum—is it a mucosal or bony change, or is it the presence of fluid? Why should an antrum be opaque in the absence of gross infection? Why are sinus radiographs less reliable in children than in adults? Is it possible to distinguish thickening of the membrane due to allergy from that caused by infection? Samuel[5] goes a long way towards answering all these questions An antrum may be opaque for many different reasons Inaccurate positioning of the patient may produce the appearance of an opacity in the antra, and certain anatomical factors may cause confusion, notably thickening of the bony walls in relation to the size of the cavity, thickness or honeycombing of the bones of the cranial vault, alterations in the slope of the normal antral walls, and overlying swelling of the soft tissues

The two factors most commonly responsible for mucosal thickening are allergy and infection A scalloped mucosal swelling, with the convexities directed towards the cavity, is likely to be allergic, mucosal thickening parallel to the walls is likely to be infective Thickening is usually greater in allergy and is often accompanied by enlarged turbinates, and polypi in the nose or antrum are nearly always allergic When the antrum is completely opaque, it is impossible to distinguish these two causes, but some help may be had from examining the other antrum, for seldom are both completely opaque If fluid fills the cavity it will be uniformly opaque, but when air is also present a fluid level is seen. Encysted fluid not under tension may form an apparent fluid level, but the absence of mucosal thickening should make one suspicious, and the lateral view will demonstrate the convexity of the "level" Thinning of an antral wall may be caused by pressure atrophy from cysts or tumours, but is also seen in the normal antrum with a well-developed alveolar recess pressure atrophy decalcifie the walls, normal thinning does not Malignant infiltration usually first involves the medial wall, but here it is not easily detected, infiltration of the lateral wall i relatively easy to detect but usually implies that th growth is advanced

A single radiograph can only show the state of th antrum at the time of exposure, the changes are ofte transient, and thus serial radiography may be essential. Radiography of the maxillary antrum only supplemen clinical examination, and should not be undertak indiscriminately, but an opaque antrum usually mea gross disease, and a clear one can nearly always be reli on as excluding it

THE WAVERLEY COMMITTEE

IN September the Ministry of Defence announced that the Government proposed to set up a small co mittee under the chairmanship of Viscount Waver F R S, "to review the arrangements for providing med and dental services for the Armed Forces at home abroad in peace and war" It has now been announ that the other members of the committee are Harold Boldero, F R C.P, Mr S R Dennison, Sir Tho Gardiner, Sir Arthur Porritt, F R C S, and General James Steele Mr E P Donaldson, of the Ministry Defence, is to act as secretary The committee me the first time on Dec 2

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[1] Scheier M. *Arch Laryng Rhin Berl* 1897 6 57

[2] Burtoff S *Arch Otolaryng Chicago,* 1945 5, 516

[3] Ballantyne J C *J Laryng* 1946, 61 306

[4] Ballantyne J C Rowe A. R. *Ibid,* 1949 63 337

[5] Samuel E *Brit J Radiol* 1953, 26 465

[6] Capps F C W *J Laryng* 1945, 60, 373.

[7] See *Lancet* Sept 19, 1953, p 615

Special Articles

THE MALADJUSTED SCHOOL

W MARY BURBURY
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SENIOR LECTURER IN CHILD PSYCHIATRY AT
THE UNIVERSITY OF LEEDS

HE present situation of schools for maladjusted child seems so deplorable and so likely to discredit their ne that it requires discussion

THE PIONEER SCHOOLS

lthough a few voluntary schools existed before 1939 did good work, it was during and after the war, partly because difficulties arising during evacuation w public attention to problem children, that the of such schools became, as it were, fashionable It taken up by the Ministry of Education and the l education authorities and was further stimulated by 1944 Act and the Curtis report. Partly because of exigencies of the time but also I think because of k of informed opinion schools have been and are ng established without consideration of the basic chological situations involved, or of the needs they expected to fulfil, without specially selected and ined staff, and (most important of all) without vision for treatment.

he first schools were started and developed by husiasts who, whatever the errors they made and atever the emotional background of that enthusiasm least brought to their work ideals warmth and a ire to understand. But as seems to happen some- es, statutory provision, by obliging the local authori to set up such schools or hostels and by limiting ir right to use (and stressing their responsibility if y use) independent schools—thereby suggesting that se are less good—has made it seem that the only portant facts are buildings staff school equipment and ng facilities. That this group of children have special eds and that since they are sick children their first ed is for treatment, seems to be overlooked.

The general public have criticised the voluntary ools for maladjusted children on the grounds that they erfere with their own convenience and rights as zens. Their objections to them derive partly from me of the more glaring errors of the pioneer school d partly from the disturbance caused in a neighbour od by antisocial behaviour the difficulties resulting m mixing of the sexes, especially among adolescents, d a well founded belief that too much freedom is not psychological antidote for earlier over repression, and at the amount of liberty that can be given to any child thout engendering anxiety and hence licence is ited. School inspectors too have criticised these luntary schools on grounds of educational inadequacies, metimes being evidently unaware of the psychological nciples which must be applied in dealing with these ildren. Matters have been little, if at all, improved by e recent provision that such a school should only be ed if the local authority is satisfied that it is suited the child, and that the child is benefiting from the ucation received there One authority felt that this ovision was *satisfactorily fulfilled by asking me to see* child whom I had never previously seen, attending a hool of which I had no knowledge whatever When I ked permission to visit the school, the authority's presentative expressed the view that the school was no concern of mine'

STATUTORY SCHOOLS

Alongside these voluntary schools the local authorities n schools have developed. These so far as my experience and knowledge go, show little sign of profiting by the earlier experiments Of all the authorities with whom I have discussed this problem, only one clearly expressed the opinion that a school should neither be opened nor kept open in the absence of good psychiatric help What seems to be insufficiently faced is that these *children are sick* by definition the schools are established for the care and treatment of the emotionally maladjusted—a term which if it means anything means the psychologically sick. No one sending a sick child to hospital for long term treatment—because he has, say tuberculosis, or needs lengthy orthopædic treatment—would question that his medical treatment must take precedence of his educational progress (though we have come to understand that schooling for such children is valuable both in itself and as part of the treatment) Nor does anyone doubt that informed medical decisions on the education of the backward must be accepted, though of course the opinion of experienced teachers handling such children may influence such decisions. Indeed, it is recognised that teachers for such children need to be specially selected, and given special training for this difficult work Yet none of these things seems to have been accepted in the case of psychologically disturbed children even though they are regarded as sufficiently disturbed to be unsuitable for outpatient treatment in child guidance clinics, and to take their places in ordinary schools

Nor has there been any real attempt to select staff Psychologically disturbed people, because of their own disturbance often have a sympathy with such children and are attracted to this work; but, also because of their disturbance they cannot furnish the stable background so essential to the child's further development. The other group of teachers, or would be teachers, who appear in such schools tend to be those who for lack of training or capacity are unable to get or keep places even among ordinary ' children Of course there are brilliant exceptions. Nevertheless one headmaster recently said to me I spend as much time trying to sort out the problems of my staff as I do those of my children

SELECTION FOR PLACES

Selection of children for the schools seems to be based mainly on expedience Thus the Ministry insists repeatedly on the separation of boys from girls—which, whatever the advantages of coeducation seems to be wise in view of the acute sexual problems which are commonly a part of emotional instability and maladjustment Heads of schools accept the importance of some selection on the basis of age-groups and intelligence and many now recognise the value of a full child guidance report—from the psychiatrist the psychologist, and the psychiatric social worker (who also reports on the home) Nevertheless, it is still possible to find in one and the same school the following types of children the relatively normal child, admittedly sent because of difficult home surroundings and only because of these the antisocial child, destructive and pilfering of the affectionless ' type, sent in apparently, because of his nuisance value, the dependent infantile child, of neurotic make up and, mixed with these more than one who suggests early psychosis among whom may be one of really dangerous, violent tendencies. Obviously it is difficult, if not impossible to run any school satisfactorily with such divergent and conflicting types. Because of the shortage of places children are sent where there are vacancies and, partly because of our lack of knowledge the suitability of the school for the child or the child for the school plays very little part in the placement.

SOME PROPOSALS

Destructive criticism is notoriously easy and it seems proper, therefore, to offer some tentative constructive ideas—though those of us who have worked with disturbed children know how often experiments need modification in the light of further experience

First, at the back of each group of such schools there should be a hospital unit, adequately staffed by psychiatrically trained personnel Interchange between the hospital ward and the school should be easy, and the hospital ward might well act as a diagnostic centre as well as a place for treatment Such a centre could send out its young patients into the schools when they were fit, and could take back into the wards any who proved unable to stand the stresses of school life Teachers might be allowed to come into hospital to instruct individual children or very small groups At the other end of the scale, the school should have a hostel for children ready to try ordinary school life, and for adolescents ready to try a job, but both as yet unready to return to their own homes A holiday centre or camp is also needed for children unable to return home for holidays, either temporarily or permanently The natural centre for such an experiment would be a university, with a medical school, offering postgraduate courses to doctors specialising in child psychiatry, and also providing courses for teachers and social workers, particularly psychiatric social workers, entering this field of work A single hospital unit, of course, could provide the medical background for more than one school, and separate schools would be planned to serve children of different ages, different sexes, different intelligence levels, and different types of problem

The researches of Bowlby, and the experience of all child psychiatrists, suggests that the commonest basic factor in emotionally disturbed children is insecurity in the early home environment, however such insecurity may be caused On this basis, various forms of illness develop as a result both of the personality of the child, and of his individual experiences Such children therefore have a common basic need for a stable background A combined scheme, of the type outlined above, would mean that throughout treatment there would be a system of continuous and cohesive relationships, and the child would experience no sudden shocks or breaks likely to cause setbacks He would himself thus have the chance to develop a capacity for stable relationships The handling of a child by one therapist throughout his treatment, and his education in one school, with continuity of discipline, must have immense advantages A capacity for relationships can never be developed by a child who is repeatedly transferred from one unit to another, however excellent such units may be in themselves

Apart from their need for a stable background, maladjusted children vary considerably, and different cases require different handling, both psychiatrically and educationally Thus the aggressive, violent, antisocial child, and the timid, phobic one, are unlikely to help each other if mixed in the same group Moreover, teachers and therapists alike find that they do their best work with one group rather than another Thus, in the interests of staff and treatment, as well as of the children, careful placement is an important part of good treatment

Children are referred for residential treatment when it is felt that outpatient treatment would be inadequate to their needs This implies that they have personality problems, for the normal child whose environment only is the difficulty is presumably placed in a boarding school for normal children By the time a child with personality disturbances is of school age, his disturbances are so fixed that he needs direct treatment for them Good environment may help, but good environment alone will no more cure his condition than it will, alone, cure a tuberculous spine Both need their special types of individual and long term treatment We spend money ungrudgingly on the 24 hour daily treatment of spinal tuberculosis Psychological treatment is sometime equally lengthy, and it ought to be in the hands o the psychotherapist True, immediate symptoms may sometimes disappear without such long-term care, bu if we are to reduce the wastage caused by psychologica illness in adult life, we must deal with something mor fundamental than immediate symptoms

In many of these cases there are problems in th home, and since the child returns there sometime during the holidays, and in any event at the end of hi period of treatment, some help should be given at tha end Whether this should be done by a psychiatric socia worker (P S W) from the clinic which referred him, o by the unit described above, may be a geographica problem The P S W of a centre which draws patient from a wide area of the country may not be able to visi often enough to give real psychological help to th parents Moreover, the P S W of the referring clinic may already have made a good relationship with them whic it would be unfortunate to break, and such a relationship is a valuable link when the child comes home for shor periods or permanently Unfortunately this kind o work is sometimes overlooked, mainly because of th demands on the service and the lack of workers, bu sometimes because the value of the P S W as a lin between the home and the school has been insufficiently understood

Someone once said " It takes a neurotic to heal neurotic " , to which another made the reply, " True but it must be a healed neurotic " Probably only person who has himself suffered from this sort of difficulty has the patience and sympathy to want to help others i the same straits, but unless he has understood an coped with his own difficulties, they will stand in th way of his full capacity to help Not all teachers want t help, or are capable of helping, these children, an no one should be expected to try unless he does so wish since the work is exacting and difficult, and demand a personal generosity which exhausts even the mos vital Staffing should therefore be generous, hours short and classes small, but over and above this, teacher should have special training in the handling of the maladjusted child Postgraduate training for experience teachers who wish to specialise is now usual, and might well be extended to teachers interested in this type o work Specially trained nurses, too, are needed in the hospital ward they need experience in child psychiatry as much as the psychiatrist himself

The scheme outlined here would not only increase the value of the service, but would reduce costs by combining in one unit a number of projects, and ensuring that staff and premises were used more economically Such an experiment might well make the title of this article a misnomer

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A SCHOOL FOR MALADJUSTED BOYS

SOMETIMES the dynamic forces which develop between parents and children rock the home The child becomes unmanageable, explodes into temper tantrums, runs away from home, truants from school, falls into delinquency, develops enuresis, or shows behaviour verging on the psychotic The parents make their own responses the mother may be worn out, anxious shrewish, or hysterical, the father irascible, brutal, or increasingly bored by the turmoil—which he escapes by going out to a public house In such a situation a diversion may have much therapeutic value

One way of creating a diversion is to place the child in a residential school for a time, with the aim of restoring him to his family when things have simmered down, and all parties have learnt a little more about the art of social living For in the event it is not merely the child but the whole family which is found to be maladjusted.

SURROUNDINGS

Bredinghurst at Peckham Rye a school for malad sted boys opened by the London County Council in 1948 conducted on lines dictated by this belief Mr W F emp, the headmaster has been obliged to develop s methods as he went along, for he had no model to py The school put at his disposal consisted of a omy house with good outbuildings, and four smaller ouses, all solidly built, standing in some 8 acres ground, at that time derelict The grounds are now easantly laid out with two large playing fields a zable pond with water lilies and goldfish, and plenty brilliantly coloured flowers, raised from seed in a ome made greenhouse

The school from the time it opened has taken its ll complement of 45 boys between the ages of six and fteen The main building holds the classrooms, a g playroom for winter and wet days and the clothing om, where boys are allowed to exercise personal taste the choice of pyjama stripes and shirts It also ontains the private quarters of Mr Kemp and his wife who supervises the clothing feeding and general are of the boys) There are also two cottages on the tate which provide a big room for art and pottery work well as another large room which is used for various urposes—cinema shows boxing and group therapy everal small rooms in these cottages are used by the aff for intelligence testing interviewing parents ffice work, and so on

The boys all live in the three residential houses, being istributed according to their age groups—little boys lder boys, and boys of intermediate age The houses re simply furnished but with an eye for colour Each f the bedrooms (most of which contain two beds) decorated in a different colour with beds and chairs ainted to match, and curtains and mats chosen to o well with the main colour scheme A bed and a hair and a share in a chest of drawers can be provided or almost any child in his own home, so the parents ave no reason to think that their child is enjoying uxuries they cannot afford. The boys eat in their wn houses, and the dining rooms too are decorated in leasant colours. The smaller boys, who need some elp sit at tables for 6 with one of the staff to encourage hem in the management of cutlery the older boys ave tables for 4 at which they can form their own groups. Each house has a playroom with some suitable equipment in the way of toys games, and books

The house matrons are experienced in looking after hildren, and some hold either a university diploma in ocial science or else the Home Office certificate in child are. They treat the children in a kind and motherly anner without trying to present them with substitutes or their own mothers Indeed the school does not ttempt, in this or any other way to supplant the parents, for the whole object is to get the child to form a better relationship with his own mother and father He orms with the school teachers and house matrons much the same relationship as a child in any other boarding school does with friendly and reliable members of the staff

THE PARENTS

It was early clear that the education of the child in a esidential school would not suffice, by itself to overcome his maladjustment the parents too, needed teaching; and they had to be encouraged to take their share in promoting his recovery In 1950 a psychiatric social worker was appointed As soon as it has been agreed that a child is to be offered a place in the school, she visits his home, for the purpose, as she explains, of telling the parents what the school is like This visit, of course besides putting her on a friendly footing with the family enables her to study the home conditions and the personalities of the parents themselves Later by her regular contact with the parents them with some of their own problems in child The parents learn that if the school their collaboration is essential Whenever are told this together—it is not left to the m the message on to a husband who at the out unreceptive, or even antagonistic, to the scho tions In the long run few parents have coöperate: for they usually mean well by their however incompetently they carry out their intentions. Parents are asked to accept certain obligations they are expected for instance to write regularly to their children to visit regularly, and if possible together and they are told that when the time comes for the child to go home for weekends one of them will be expected to come and fetch him on the Friday night and bring him back on the Sunday and that it is important not to break these engagements for trivial reasons or without giving warning Of the parents of the 150 children who have already passed or are passing through the school very few have failed to do their share in these ways and only about 5 have flatly refused to attempt it

PSYCHOTHERAPY

In the school the child is not only taught in the ordinary sense, but is given whatever psychological help he needs. As soon as he is able to profit by it, individual psychotherapy gives place to group therapy, which is proving very useful One of the psychiatrists attached to the L C.C holds regular sessions twice weekly in the school a lay psychotherapist attends five days a week, and an educational psychologist is also attached to the staff. Thus there is a full child guidance team working on the premises and in close collaboration with the school staff—an arrangement at present unique in this country The child's maladjustment can in fact, be studied at one and the same time from the psychiatric the educational, and the social aspects Case conferences are held by the staff every week when the child's progress is discussed and assessed

If the parents are young and willing to learn they too are asked to come and see the psychotherapist and as a result a good deal of teaching is given in the principles of mental health After the child's first few weeks in the school he is allowed to go home for every other weekend and the children all recognise this as a first step towards going home for good His parents fetch him on Friday evening and return him on Sunday evening when the headmaster the psychiatric social worker, and the house matrons are there to receive them, and to have a talk about the children The link between the school and the parents is thus very strong

THE CHILD'S PROGRESS

In school the children do a good deal with their hands —painting, modelling Meccano the making and baking of pots and the construction of glove puppets. Every child is taught woodwork in an out-house dedicated to the purpose, and he is allowed to take home his constructions—aircraft simple bookcases and the like—to keep at the end of the term Apart from this, the staff give much serious thought to the teaching of reading, for nearly all these children have great difficulty in learning to read However as soon as a child manifests an interest in books the teachers follow it up and help him to master reading by whatever method seems to suit him—phonetic, look and say or even the time honoured C A T cat system, which some children seem to prefer

Once a child is responding in the classroom, and is beginning to overcome his emotional problems, he is allowed to attend the local primary or secondary school and wears cap and blazer of that school like the rest. is recognised by the children as an advance in ds going home for good The school usually t s half the children on the roll every year, and in ive years since it was opened 99 have gone home oved—in most cases to homes which have also roved Some 80% of those who have been discharged or two years and over were going on satisfactorily at follow-up

It seems that Bredinghurst goes far towards fulfilling the criteria for schools for maladjusted children set out by Dr Mary Burbury on p 1251

THE WORK OF C I.O M S.

THE Council for International Organisations of Medical Sciences was founded in 1949, under the joint auspices of W H O and UNESCO (At first it bore the name of Council for the Co-ordination of Medical Science Congresses) By acting as a registry office for international meetings C I O M S obviates the clashing of dates, and it is often able to persuade organisers to group their congresses so that interested persons can attend more than one Thus a congress on cardiology has been arranged in juxtaposition to one on internal medicine, a congress on cancer was timed in conjunction with one on radiology, and psychiatrists were able to attend consecutively congresses on mental health and criminology as well as psychiatry

The Council has also organised a number of important symposia, often at the time of a congress In 1952 four of these were held on experimental diabetes, the pathogenesis of arteriosclerosis, cancer of the lung, and hæmophilia These informal international round-table conferences are of special value in that they may be held in distant centres which are not always convenient for the staging of a major convention A logical development from the international congress and symposium is the organising in the same place, immediately before or afterwards, of an international postgraduate course, so that full use can be made of the services of the world leaders of the specialty who have congregated The Council has now arranged several such courses

The Council gives financial aid to international congresses for the initial organisation and also for securing speakers who might otherwise be unable to attend [1]

PLANNING A CONGRESS

In September, 1952, a conference took place in Paris of key officers of recent international congresses, and their findings are included in an account of the planning and organisation of such meetings [2]

The first international societies came into being at the end of the last century More recently such societies have tended to develop into instruments of research, enabling men with different national backgrounds to work side by side

Thus the social side of a congress is as important as the scientific side "Congressists" should be encouraged to get to know each other early in the meeting There are many ways in which organisers can help to achieve this end Buffet suppers, for instance, are preferable to sit down dinners, because they allow of more mixing, while evening dress should be optional and receptions free so that no one need feel unable to attend

The Council urges that the international society responsible for a congress should determine the pattern of the congress and the main subject to be discussed, although obviously it is seldom possible for the society to work out all details and select all the speakers, much of this work is better left to the local committee, which must, however, take care that the host country does not appropriate more than its share of the programme The secret of good congress planning is to plan early, for all local organisers learn, often to their cost, that international correspondence is slow The establishment of national committees to screen all material offered to the congress is an excellent way of securing international coöperation.

The president or chairman of the local group and the secretary-treasurer are the key officers, but their exacting work can be greatly eased if subcommittees play their proper part the two most essential ones are the programme and the social-functions subcommittees. A competent secretarial staff should be engaged early on and at once be allotted adequate space, for near the time of the congress it is inconvenient to move a growing secretariat into new premises A stipendiary executive officer fully conversant with congress technique can be a boon to the organiser of a big congress, but he cannot have the same knowledge of the personalities of participants as has the amateur who elects to run the congress for his professional colleagues

Nowadays a popular form of congress pattern consists of principal papers from invited speakers ("rapporteurs"), followed by critical or even contradictory papers from other distinguished leaders who have enjoyed a preview of the "rapporteurs'" contributions, before general discussion is permitted An alternative is to have invited and proffered papers grouped appropriately and each followed by discussion. Discussion has been found to be at its liveliest, however, at open symposia, especially when these are not too large, here a given topic is discussed by a panel of experts before an audience which is entitled to take part in an exchange of views At all congresses, however, an opportunity should be given for all to speak, especially since at present some members are only allowed by their employers or government to attend if they contribute to the meeting The reading of papers in title only is to be deprecated, because some of these papers may deservedly provoke a good discussion If necessary simultaneous sessions should be employed to exhaust the agenda The suggested time for a proffered paper is ten minutes, with five minutes for a discussion 1000 words can be delivered in ten minutes, but each lantern slide, if explained, must be reckoned as the equivalent of 50 words

Abstracts are essential, for they not only enable national committees to evaluate the papers but allow of translation into other languages It is recommended that the closing-date for the receipt of abstracts, which should not exceed 200 words, should be six months before the congress

Visual aids, such as the cinema and television, should be encouraged, they help greatly to minimise the ever present language difficulty The scientific exhibition, or demonstrations, encourages direct exchange of information and the making of valuable contacts The trade exhibition, too, is valuable, for the renting of space can be an important and legitimate source of congress revenue.

The greatest anxiety and expense for the organiser is over interpretation For small meetings, and especially those confined to two languages, the consecutive technique is suitable and has the advantage of not requiring expensive equipment For big meetings, however, simultaneous interpretation, if carried out by experts, is to be preferred But the interpreters must not only be excellent linguists they must be experienced in medical terminology Indeed, they should study the papers in advance

C I O M S has valuable advice to offer on the more technical points of congress advertising, budgeting, enrolment, registration, and programme printing. Hotel accommodation is best left in the hands of travel agencies, but hostel accommodation and private hospitality should be provided and encouraged.

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[1] C I O M S Bulletin 1952, 3 no 1–2 The editor's office is at Unesco House 19 Avenue Kléber Paris 16e Annual subscription 9s or $1 60 no payment required from universities medical institutes or medical organisations.

[2] Ib 52 3, no 3–4

A special section of the report deals with the psychology international gatherings Every effort should be de to make visitors feel at home, and interpretation uld be provided not only at the scientific meetings but at the formal parties and excursions. All countries uld have an opportunity of *providing* chairmen and ing speakers. While not all may agree with the ous anthropologist who said that the makings of a d congress are music flowers and flags, most will nowledge that its success does not depend only on the ntific fare.

OTHER WORK OF C.I O M.S

The funds of C I O M S are derived from W H O sco, and the supporting societies. Half of the enue goes on grants for congresses and a fifth is roted to financing symposia and advanced courses w projects are envisaged by the Council, which now is ready to undertake greater responsibilities in the d of international medical science For instance, this r it has published a directory of the international anisations of medical sciences.[3]

The first part of the directory lists all international non ernmental organisations under subject headings. The ond part gives the national associations affiliated to each rnational organisation.

It is also responsible for the setting up of an inter tional commission on anatomical nomenclature and gave financial support to a similar body on cancer menclature. At present it is engaged on the mpilation of an anthology of psychiatric usage, while ently it, convened a meeting of senior executive icers of national research organisations to discuss the ruitment training, and careers of research workers the medical sciences But perhaps its most ambitious dertaking will lie in the direction of trying to egrate medical bibliography and literature and more rticularly indexing and abstracting A joint meeting the C.I O.M S UNESCO and W H O is to be held ortly to discuss medical documentation ' and to termine which problems are suitable for international tion and in particular for action by C I O.M.S

WELLCOME RESEARCH LIBRARY

Development at the Royal Society of Medicine

ON Dec. 4 Lord Woolton in the absence owing to illness the Marquess of Salisbury opened the Wellcome search Library of the Royal Society of Medicine

Sir FRANCIS WALSHE, F R.S the president of the ciety paid tribute to the foresight and generosity the Wellcome Trust It was a remarkable achievement r a small body of private people to establish a library over a quarter of a million books and to provide for s maintenance, growth and services out of their own sources. But the library had outgrown the society s rength and the gift of £125 000 from the Wellcome rust was timely

Sir HENRY DALE O.M , F R.S chairman of the Wellcome rustees and a former president of the society recalled ow the trustees *first helped the society with a gift* f £30,000 for additional library accommodation after e second world war Since then they had given a rther sum of £45 000 and for the next ten years the rust was going to pay the subscriptions of some 300 Vellcome associates, chosen among young graduates ho would not otherwise be able to afford the sub ription. Many of those already elected were young rseas graduates studying under the British Post graduate Medical Federation Though a permanent ution had not been found for all the problems which ed the society Sir Henry was sure that the library which was a national and imperial posse be allowed to be lost.

Lord WOOLTON was impressed that occupants of chairs " used the library o that provincial members borrowed 80 000 year *With 5000 volumes a year being adde* see there would be difficulties ahead The Govern ment is much concerned that the findings and records of scientific advance should be made as widely available as possible through the adequate service of technical libraries, ' he continued ' The Lord President s office is considering various ways of meeting the present specialist library requirements " The library would become an increasing strain on the resources of the society already it was costing about £25 000 a year It might well be that before long the society would wish to consider associating itself with other more general schemes for the supply of scientific literature which the Govern ment had in mind. It seemed inevitable that the many interests in this field must agree to collaborate if the public needs were to be met within the financial resources, not only of the society but of the country Any vast project for a new national medical library was bound to be extravagantly and even impossibly expensive Collabo ration was better than competition and the Government would welcome the opportunity for discussion when the time was ripe

A vote of thanks to Lord Woolton was proposed by Lord WEBB JOHNSON chairman of the building com mittee and afterwards Lord Woolton and the guests inspected the new library

The architects are the late Mr J J Joass, F.R.I B.A. (who designed the original building) and Mr Leslie Watson, F.R.I.B.A

HEALTH RESOURCES IN THE UNITED STATES

THE Brookings Institution has been responsible for a number of long term studies on health and welfare in the United States. Anyone who doubts the value of statistical inquiries will do well to read a study from this institution on health resources.[1]

This investigation was undertaken with several objec tives in mind including the ascertainment of the extent of health resources, the description of major private and public health programmes, and the establishment of a basis for further study Dr George W Bachman and his team have divided their survey into three parts concerned with (1) the health of the nation, as shown by vital statistics (2) the personnel in the health services ; and (3) these facilities and services

STATISTICS

Between 1900 and 1950 the death rate dropped nearly 45% and life expectancy increased almost 37% The death rate for infants under 1 year dropped from 162 4 per 1000 live births in 1900 to 31 3 in 1949 The investi gation shows clearly the effects of increasing age for more than half the hospital beds in the United States are for long term chronic illnesses The diseases in respect of which the death rate has increased are primarily those of middle and later life

Returning for a moment to the infant mortality rate for every 1000 babies now born some 130 live who would have died fifty years ago It is also known that of the thirty or so deaths which *did* occur among those babies, at least a fifth were preventable in the light of present knowledge—in some areas of the country infant death rates are consistently at least a fifth below the national average, while in others they are consistently above the national average.'

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[3] Ibid 1953 4 no 1-3

[1] Health Resources in the United States Personnel Facilities and Services. GEORGE W BACHMAN and associates. Washing ton, D C Brookings Institution. London Faber & Faber 1953 Pp 344 36s.

s, however, in the variations in level of health by rict, sex, and colour that the statistics are most vealing Non-white males, for example, have a much higher death-rate for vascular intracranial lesions, chronic nephritis, tuberculosis, diseases of the respiratory system, syphilis, and accidental death Non-white females also have high rates for the same conditions, except accidental death The Southern and South-western States have the highest mortality-rates, and in relation to population they have the fewest hospital beds and medical personnel The three northernmost New England States—Maine, New Hampshire, and Vermont—have a high percentage of old people in their population and a relatively low birth rate

It would be interesting to know what some of our maternity and child-welfare experts would say of the following conclusions

> "In the great majority of cases, births which take place in hospitals are less likely to result in death to either mother or infant The hospital delivery to some extent reflects a total pattern of care or a non hospital delivery reflects the absence of that pattern mothers who give birth in hospitals are more likely than others to have had some prenatal care and hence are less likely to be delivered of stillbirths, they are more likely to receive continued medical care, with less chance of death to the infant in the first year of life"

It is also noteworthy that over one-tenth of all infant deaths in 1949 occurred within the first hour of life, and the data on urban first hour death-rates indicate a sharp difference in mortality risk for babies born in hospitals and babies born outside of hospitals, even though in the United States as a whole some 95% of all live births in 1949 were attended by a physician Indeed it is in the use of midwives that the greatest difference between the U S.A and this country is evident In thirteen States in 1949 the proportion of live births delivered by a midwife was less than 0 5%, and in three States none was so delivered In one State—Mississippi—the figure was 20 1%

In the Pacific States of Washington, Oregon, and California the percentage of infants born in hospital reached the extraordinary figure of 98 6 in urban areas and 97 1 in rural areas The study of maternal mortality statistics also brings out clearly the differences between rates for non-whites and whites "Among the whites about one woman age 20 to 24 died as the result of pregnancy per 2000 live births, whereas among the non whites the ratio was about one in 500" The death-rates for infants of 1–12 months were 8 7 per 1000 live births for whites and 17 4 per 1000 live births for non whites

The American investigators use the term "immature infants" to describe those born either too soon or with a significantly subnormal body weight, and it is estimated that 5–11% of live births fall in this category In 1949 the estimated death rate resulting from immaturity was 16 5 per 100,000 total population, making it one of the major causes of death in the nation The rates for non-whites were almost exactly double those for whites Nearly all the States require a record of the infant's birth weight on the birth certificate

The morbidity studies show that women are more often ill than men, and that chronic diseases are responsible for a very high proportion of the days of disability The figures also show that the disabilities of persons 65 years of age and over arise primarily from chronic illness In the words of the authors

> A country with an aging population must look forward to a constantly increasing aggregate number of persons disabled by illness for 12 months or more unless it can achieve success in combating chronic illness and the degenerative diseases '

In 1947 Blue Cross participants on the average went to the hospital more often than did the highest income class of whites in 1928–31 The factors involved are (1) increased hospital facilities, (2) transfer to hospitals of many cases previously cared for in the home, and (3) the tendency of insurance plans to encourage hospitalisation

PERSONNEL

Health personnel increased by about 40% between 1940 and 1950 Physicians increased by 17%, auxiliary nursing personnel by 98%, psychiatric social workers by 35%, psychologists by 166%, and sanitary engineers by 129%

> "One of the results of the uneven rates of growth [for different professional groups of health personnel] is that the major professionals make up smaller proportions of the health labor force than ever before Physicians, for example, who accounted for about 20 per cent of the 1940 total dropped to 16 per cent of the 1950 total Professional nurses also decreased, from 30 per cent. in 1940 to 26 per cent in 1950 In contrast to these decreases was the proportionately large gain in auxiliary nursing personnel, from 21 per cent. of the 1940 total to nearly 30 per cent of the 1950 total"

Of the *physicians,* 36% are general practitioners, 11 4% are general practitioners with part-time specialties, and 27% are full time specialists "Full time" in this connection means those whose practice is limited to a specialty Between 1940 and 1949 the number of full time specialists increased by 70%, while the proportion of general practitioners, including part time specialists, declined by about 13% The median age of physicians in 1948 was 44 4 years

In the United States there are 86,870 *dentists,* of whom 95% were in active practice in 1950 Only 3 1% of these were in federal government service Recognised dental specialties include orthodontics, pædodontics, periodontics, and prosthodontics, in addition to oral surgery, oral pathology, and public-health dentistry The mean age of dentists was approximately 48 years, and, although the dentists in the year sampled (1949) were older than those investigated in 1940, "continual improvement in techniques and increased use of dental hygienists and other assistants probably resulted in greater productivity"

The most dramatic changes are in the "*other health personnel,*" such as dietitians, laboratory technicians, medical record librarians, medical social service workers, occupational therapists, physical therapists, practical nurses, and X-ray technicians The over all increase in the group described under this heading is 70% in the years 1940–50 The vacancies in the eight categories numbered almost 47,000, with an estimated additional 77,000 needed in the next five years

Mention has already been made of the decline in *midwives,* their numbers dropped from 62,000 in 1923 to 18,925 in 1950 "The downward trend is attributable to the improvement in economic status of the population, enabling the use of medical and hospital services in preference to midwives, and the increased stringency of licensure" Nevertheless, "the midwife remains indispensable in areas where medical and hospital facilities are lacking" Most midwives practise in the South and among non white members of the population living in rural parts More than a third of all midwives in the United States were in Texas, Mississippi, and Virginia.

Dental hygienists numbered 7000 in 1950—an increase of 40% over those employed in 1940—and it is computed that at least 15% of the volume of dental services could be performed by hygienists

In 1950 75,000 *social workers* were employed, of whom 3000 were in the field of general medical care and 2250 in mental hygiene But in 1940–50, whereas the number of social workers in a general medical setting increased by only about 21%, the number of social workers in the psychiatric or mental hygiene setting quadrupled

Dietitians and nutritionists formed an important group numerically, but their importance is shown in another way, for the American College of Surgeons requires the food services in hospitals they approve to be administered by a person who meets the requirements of membership of the American Dietetic Association The function of public health nutritionists is defined as primarily to impart the principles of good nutrition to groups which in turn reach the public *tometrists*—i.e., specialists in the conservation and ovement of eyesight—increased by 71% in the ten years. e average case load of *chiropodists* in 1949 was 26 patients day for 220 days per year and an estimated total of 0 000 patients were treated during 1950

rhaps the most startling difference is in the status of *paths* for in 34 States and the District of Columbia graduates of colleges of osteopathy are eligible to be sed to practise medicine including drug therapy and ative surgery; in all but two States they are licensed practise obstetrics. An examination of the case-load a week in May 1950 showed that nationally there during that week 74 3 patients and 85 0 visits per opathic physician.

iropractic is a system of mechanical therapeutics con ng of a search for vertebral dislocations and, if found reduction by manipulation to relieve pressure on the es. *In 19.0 there were approximately 1500 chiropractors* ctive practice.

terinarians figure prominently among the health personnel the reasons are set out under four headings. Firstly veterinarian contributes to the control of animal diseases smissible to man; secondly he helps to maintain the ant high nutritional level of the American people by rolling the health of food producing animals; thirdly military veterinary services protect the health of the ed Forces by inspecting food for wholesomeness and ity and fourthly many fundamental discoveries in icine have come from the veterinarian—for example umarol and B C G

anitary engineers have doubled in number since 1940 about half are in public employment. Their duties include community planning the design and operation of water sewage, and industrial waste treatment plants and many other duties which in Britain fall to the medical officer of health and sanitary inspector

CARE OF THE AMERICAN INDIAN

One of the most interesting parts of this book is the section dealing with the care of the 400 000 American Indians. In 1789 the War Department was given control over Indian affairs, and the Bureau of Indian Affairs was established in 1824 From about 1832 Congress voted a sum of money annually for the prevention of disease among the Indians and in 1849 the responsibility for medical care was transferred to the Department of the Interior Since 1924 all Indians have had citizenship rights, but the federal government has continued to provide medical services for the indigent, and, because of their general economic conditions, most Indians are eligible Indian health problems are significantly different from those of the general population "The major problems are tuberculosis high infant mortality rates, diarrhea and dysentery, trachoma poor nutrition and dental caries.' The incidence of tuberculosis is very high indeed

In many instances the hospital staff consisted of only one physician per hospital and most reservations have only one nurse In many places, because of the language barrier, each public health nurse must have a driver interpreter

Public Health

Action against Smog

N interim report [1] by the Committee on Air Pollution Beaver Committee) was issued last week when Mr rold Macmillan Minister of Housing and Local Govern nt, made a statement in the House of Commons p 1200).

The report recommends the following main precautions be taken immediately

. Warnings to be issued by the Meteorological Office in ticular through the B.B C, of areas of normally high lution in which serious fog is expected to persist for at t 24 hours.

. Advice to the public and industry on action to alleviate mog and its effects Nearly half the smoke comes m house chimneys and about an equal amount from ustry

The committee urges that householders in large towns o depend on solid fuel and who normally burn coal uld lay in a stock of say a hundredweight of coke other smokeless fuel for use in periods of persistent . A mixture of coke and coal will burn reasonably ll and will greatly reduce smoke When persistent g is forecast

1 Householders who can use only coal should take special e not to make more smoke than can be helped. Fires ould not be banked up at night

2. Those who can use smokeless fuels should confine them lves to those fuels during periods of fog

3. Rubbish should not be burnt nor bonfires lit while the g lasts.

4. The general public should refrain from bringing motor hicles into densely populated areas.

5 Less smog' will find its way indoors and rooms will kept warmer, if draughts can be prevented

6 Elderly people and those suffering from chronic chest d heart conditions would be well advised to keep indoors d to rest as much as they can if the fog is very thick. If ey must go out they will find that a closely fitting simple ase mask, or even a woollen scarf wrapped round the mouth and nose, will give some relief by filtering out some at least of the solid contents of "smog

Regarding industry the committee recommends that smoke-control measures should be brought up to peak efficiency at once and checked frequently throughout the winter, that special efforts should be made to prevent heavy smoke when stoking and that a continuous check be instituted against the emission of dark smoke This check can best be made by installing a simple smoke-density indicator

The report remarks that it has been estimated that in the London smog of last December up to 60% of the smoke was due to domestic fires "It follows that a first immediate and stubborn obstacle to the reduction of smoke is the preference of the majority of people for traditional methods of heating The need for education and training in these matters is urgent and vital

'It is, says the committee simply a question of balancing the cost and inconvenience of enforcing a more efficient and scientific use of our fuels against all the advantages to be obtained in health, convenience and economy from a clear atmosphere This problem with all that is involved in a real attack on the menace of air pollution, is one which must be faced

Infectious Diseases in England and Wales

Disease	Week ended November			
	7	14	21	28
Diphtheria	18	26	28	16
Dysentery	358	370	363	[illegible]
Encephalitis				
Infective	10		6	1
Postinfectious		1	1	
Food poisoning	138	104	132	121
Measles excluding rubella	1030	823	703	876
Meningococcal infection	[illegible]	36	30	32
Ophthalmia neonatorum	26	37	25	20
Paratyphoid fever	8	1	9	3
Pneumonia primary or influenzal	507	531	584	657
Poliomyelitis				
Paralytic	60	66	[illegible]	59
Non paralytic	34	29	31	37
Puerperal pyrexia	205	216	213	211
Scarlet fever	1187	1100	1613	1384
Smallpox				
Typhoid fever	3	1	2	2
Whooping-cough	2173	2410	2510	2603

Not including late returns.

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[1] Interim Report of the Committee on Air Pollution Cmd no. 9011 H.M. Stationery Office Pp 31 1s 0d.

In England Now

A Running Commentary by Peripatetic Correspondents

MY gardening diary says that this is the time of year to take stock of the gentle art, to make a critical post-mortem examination of last season's living beauty, and to conceive the embryo of next year's brilliance But the diary reckons without the hazards of country life Paragraph by paragraph we punctuate the text with hollow laughter

Prick holes in the lawn to aerate the turf, says the diary, fill in the craters dug by the dogs, we reply Your lawn can be greatly improved by spraying with the new hormone weed-killers, runs the book, we could tell them a thing or two about hormones on grass, lovely green rings of succulent turf where the bitches have squatted, in fertile contrast to the withering squirts of the dogs

Vivid memories spring to mind The puppies chewing off the daffodils, rolling flat the stocks, the cats finding easy digging in the seed-beds, the mice rooting up the peas, and the hens scattering the polyanthus with those disdainful back-thrusts reserved for all inedible obstructions The rabbits' lolloping breakfasts along the dahlia rows Wire your garden against rabbits, says the diary, shiver at dawn in your pyjamas by the bedroom window with a 22 rifle, we sadly reply

The winds of March bring more than the daffodils They bring the hungry in-lamb ewes down to the home pastures Not even a five-foot dry-stone wall will stop their quest for greenery Prune your plants well back for vigorous growth, says the text, grant that the nibbled stumps will revive, we pray But worse has yet to come, the silly beasts panic into the roses, entangle their fleeces on the thorns, and avulse the entire bushes, roots and all One fat ewe carried for weeks on her rump the proud label "American Pillar" as she trailed our five bob's worth in open mockery

Then the cows come out to grass—our grass and our vegetable garden Cows in the garden can lick bulls in china shops any day They are most unpleasant at both ends. For one thing, they have such an enormous axle-load that all our lettuces are plunged irretrievably into the depths, and we are left disconsolate with a pock-marked wilderness As a final gesture the creatures charge through the raspberry canes, emerging festooned with a tangled wreckage of plants, wire, and bamboo Their owner hopes that they haven't been poisoned by eating our yew trees We favour wing of bat.

What remains of the garden then qualifies to endure the onslaught of footballs, cricket balls, tennis balls, and arrows, lethal not so much per se as by their attendant propensity for getting lost. The grooves of tricycle wheels snake across the lawn, the ends bearing witness to televising dirt-track technique From such memories our green fingers close the diary with foreboding We breathe a silent prayer of thanks that no-one near keeps pigs

* * *

It has been hinted that the new examination technique, recently described in this journal, may have an effect on future graduates and as one who believes in keeping upsides with medical progress, I have already introduced the new doctor-patient technique into my practice Last night, for instance, as my patient hobbled through the surgery door, I snarled "You want—Indicate with a cough your reason for coming here tonight

(*a*) A certificate, tonic, line for glasses and a roll of cotton wool for wee Jeannie
(*b*) To get in out of the rain
(c) A check up going over, sounded, given the once over and a smog mask
(*d*) Nobody else will talk to you"

Silencing his feeble tale I resumed "Have you
(*a*) A cruel pain
(*b*) Something you can t describe but comes often especially at night what with the neighbours and all
(c) Blackouts and coming all over queer
(*d*) A gastric stomach"

We were progressing I continued "Is the pain
(*a*) Round the back, working to the front and you're afraid you'll be taken serious if they meet
(*b*) Something horrible when you bend
(*c*) There because the foreman has a spite at you and put you to heaving coal which is Joe Bloggs's job by rights"

Barring his exit I urged him to answer quickly "true" or "false" to the following questions
" (*a*) You wish you'd stayed at home
(*b*) You feel much better
(*c*) Doctors are grossly underpaid"

I met my patient in the street this morning and he looked at me queerly, but I suppose medical pioneers must expect some setbacks

* * *

Women can be annoying creatures I had just finished re-reading some of the Sherlock Holmes stories and was explaining to my wife that Holmes was based on a well-known doctor I related a few examples from my own experience to illustrate the deductions that might be drawn from fine observation At that point the telephone rang "That'll be Millie," said my wife rising to her feet "I know her ring" Later, when I was patiently inquiring how she could differentiate a telephone bell, our door buzzer sounded "Oh," she said, "that's Jim and he sounds cold" It was Jim, and he was cold I went back to my stories, but somehow they had lost their flavour

* * *

As a conscientious M O H, I have been put in a quandary Shall I or shall I not advise my authority to accept the Ministry's latest suggestion and offer B C G vaccination to school-leavers? If B C G is good for contacts, it may protect children when they leave school for the wider world of exposure On the other hand, I am coöperating in the M R C trial to find out how worth-while mass vaccination of this age group is. To take action now is rather assuming an answer before the result is known I was mulling this problem over in my head yesterday evening while I read my son to sleep with *Through the Looking glass* Later, drowsing myself, B C G and the book began to get mixed up

"Does B C G work?" asked Alice "In some people," the Duchess replied, "but we've arranged a trial to see if it would be useful in school children" "How long will the trial take?" Alice inquired "About three years," answered the Duchess Looking around, Alice noticed crowds and crowds of children carrying cards She asked who they were "Those are school children being given B C G," said the Duchess, "every one of them can have it" "But I thought you were having a trial to see if it would do them any good," said Alice, puzzled "That's quite right, my dear," rejoined the Duchess, "but you see we're having the verdict first and the trial later" "Very interesting," commented Alice, as she went to get her own card

* * *

I am often glad that my duties do not include teaching, but then I always have been the sort of chap whose experiments never quite came off Recently, having been asked, we explained to our three children that human babies, unlike kittens, were born with their eyes open With my luck in these matters I might have suspected that facial œdema would keep our new arrival's eyes closed for four days

* * *

She would none of all your posies ?
Bade you gather her blue roses ?
What a curious neurosis *

Half the world you wandered through
Seeking where such flowers grew ?
Really, what a thing to do

Cases both, quite obviously
You, more fortunate than she,
Made a good recovery

Tell me now did you enlist
The aid of a psychiatrist,
Or spontaneously untwist ?

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*R Kipling's description of this case appears in *The Light That Failed* p 033 —ED L

Letters to the Editor

THE INSULIN MYTH

ir,—An E C T myth appals me! I must disown it d explain that to ignore E C T when discussing insulin impossible, for to repeat it is so often mentioned just another manipulation of the insulin-coma ritual. wanted to make clear that my target was insulin d that such dubious benefits as physical treatments ffer in early schizophrenia could more safely and eaply be obtained by E C T

Its effect is unique in the chronic malignant variety ile relapse and remission within a few days of with awal and re application are familiar with E C T and known with insulin, these points were cited to pport my view and as an indication possibly, of some ecific value To avoid more red herrings across the ll of insulin I must as he will understand leave answered here Dr Hunter's objections (Nov 28) my unscientific attitude to E C T On other points impressive support and that of Dr Gibson (Nov 21) d Dr Jarvie (Dec 5) is most pleasing

As for the extraordinary misconstruction that Dr nford Rees (Nov 28) makes of my article which he kes to be a special plea for E C T based on a series of my n, it will be recalled that these figures mentioned in ssing, in a bare dozen lines were given simply to suggest at the prognosis of early schizophrenia may not be quite black as is often assumed. They gave no support atever for E C T or for any treatment at all Further, these same lines, and as the subject of a whole para aph later I discussed the time factor relating response treatment. Thus Dr Rees accuses me of ignoring

The insulin myth is, I think so well demonstrated by r Mayer Gross's work[1] I am sorry now, that I did t refer to it because of certain details. My reason r this was that at least half his 454 cases at Dumfries ere given adjuvant E C T—a point he does not mention his letter A significant indication was failure to prove after three or four weeks of insulin comas; d, of those with lasting improvement, some 65-70% d had E C T Though this objection to this series oving any worth for insulin is enough the optimal ntrol group he refers to for comparison is also not ove criticism It consisted[2] of voluntary patients the Maudsley in 1935 and it is widely held that luntary patients, with their less florid symptoms and idious onset, have a worse prognosis[3] Dr Mayer ross and his colleagues actually indicated this, and plained that there were difficulties in accommodating ute cases.

The work on conditioned reflexes in rats and on etabolism, from which Dr Mayer Gross draws a tisfying rationale for the use of insulin in a human ental illness with no known metabolic pathology not, I think, satisfying enough to justify a risky eatment otherwise so ill founded.

To question a myth is to invite counterblast as well criticism including of course Dr Sargant's conviction hat truth resides with majorities. I think he misquotes ov 28) a report to the International Congress in aris This report was by Lopez Ibor[4] and not by Seven, at all events it made clear that the value of nsulin might reasonably be doubted and suggested that C.T was preferable to insulin in certain types of schizo phrenia. Dr Sargant's concern for the suffering my rticle may cause will be all the greater if he reaches for a standard textbook[5] and reads the very lukewarm opinion of insulin there, and for the most authoritative book[6] on physical treatments in the language, where he will find little to choose between E C T and insulin in acute schizophrenia This evidence would perhaps encourage Dr Friedmann (Dec 5) to be less certain that it is I who ignore what I dislike and that he has proved the value of insulin while combining it with E C T

Dr Rees and Dr Sargant seem to accuse me of "selecting" my references I made it clear why it was necessary and possible to consider ' only some of the best known careful, and typical reports" This is what I did and, in fact, the missing work for which they plead contains not a single revelation that is absent from the papers I dealt with Moreover, work supporting my case was omitted some of which Dr Mayer Gross kindly pointed out Of the 9 omissions they deplore they have only 3 in common the work of Dr Mayer Gross Freudenberg a paper[7] of whose I mentioned with the brief comment it seemed to require and Finiefs[8] Had I included those papers they name they could readily have found many others, all saying the same thing, with which to reprove me

Though I drew attention to the question of percentages, I see that Dr Rees still reaches conclusions by converting unimpressive small numbers to percentages when he refers to an 8·4% recovery rate with insulin compared to zero with E C T in long-standing schizophrenia[9] Actually this means 2 patients out of 24 nor were they the hospital chronics I talked about, while the social recovery rates in his groups which his letter did not mention were not significantly different This distinction between cure ' and social recovery is always subjective

I make no apology for confining myself to published evidence and ignoring the impressions of clinicians, many of whom have no experience of other approaches to schizophrenia and who use insulin and are often encumbered by many years of it. That they will go on doing so undaunted, does not surprise me for there are so many other intuitions and myths dominating psychiatry

Others matters raised in this correspondence are I think answered in my article but I must comment on Dr Sandison's enthusiasm for his new insulin unit (Nov 21) To take his own figures in whole numbers (which I prefer to percentages) it seems that in a fair sized mental hospital with a small medical staff, perhaps less than ten schizophrenics, in nearly two years, have made some sort of recovery so far brief and *perhaps* attributable to insulin—this at the expense of one treatment death

Can anyone, who is not possessed by furor thera peutica, as Freud called it, and not hypnotised by palaver, syringes, coma and the terror of therapeutic impotence, really believe that the risk and great expenditure are worth it?

Fountain Hospital,
London, S W 17

H Bourne.

RADIOACTIVITY OF TOBACCO AND LUNG CANCER

Sir,—Mr Mulvany's letter of July 25 suggests that natural potassium may have to be added to the list of ' radioactive carcinogens, of which only certain products of the radium and thorium series are so far known to have produced cancer in man[10] The specific radio activity of potassium[11] however, is at least 10^{10} times less than radium and its energy dissipation in tissues 10^{11} times smaller than that of an equal radium con

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1. Mayer-Gross, W J *ment Sci* 1951, 97 132
2. Guttmann, E., Mayer-Gross, W., Slater E. T O *J Neurol. Psychiat* 1939, 2, 25
3. Kalinowsky L. B., Worthing H J *Psychiat Quart* 1943, 17 144
4. Lopez Ibor J J International Congress of Psychiatry Reports, Paris, 1950; vol. 4, p 92
5. Henderson, D K., Gillespie R. D A Textbook of Psychiatry London, 1950 p. 415.
6. Kalinowsky, L. B Hoch, P H Shock Treatments, Psychosurgery and Other Somatic Treatments in Psychiatry 2nd ed., New York, 1952
7. Freudenberg, R K *J ment. Sci* 1947 93 9
8. Finiefs, L. A *Ibid* 1948 94 575
9. Rees, L *Ibid*, 1949 95 625
10. Loutit, J F Progress in Biophysics. London 1950 p 107
11. Burch P R. J *Nature Lond* 1953 172, 361

centration. Other factors will enter into the consideration of a given biological action, but such differences in physical properties suggest that a quantitative assessment of the possible dose to lung tissue should precede any conclusion that the radioactivity of the potassium content of tobacco plays a part in the ætiology of lung cancer.

The accompanying table gives results of testing the tobacco, ash, and condensed smoke of a number of samples of cigarettes in a Geiger counter of the type (M6) used by Mulvany. It will be seen that the counting-rates obtained for the cigarette ash are of the same order as those reported by Mulvany, but in this case the counting-rates have been converted to equivalent weights of potassium by calibrating the counter with potassium salts. Assuming the observed radioactivity to be due to potassium, the table gives the activity in equivalent weights of potassium per cigarette, both as tobacco and as ash. The values for the tobacco and ash are sufficiently alike to suggest that no radioactivity is lost in the process of smoking. This suggestion is corroborated by measurements on a solution in acetone of condensed unfiltered cigarette smoke kindly supplied by Dr Clayson from the smoking machine in the Department of Experimental Pathology and Cancer Research. The conditions of this measurement favoured sensitivity, since the condensate from some 300 cigarettes was contained in the counter. No activity above background, however, could be detected in a long series of counts and the figure of 6 µg "potassium" per cigarette in the condensate is the maximum likely figure assessed from the standard deviation of the measurement.

RADIOACTIVITY OF TOBACCO, ASH, AND SMOKE

Sample	Observed counts per min.		Potassium per cigarette in mg	
	Tobacco	Ash	Tobacco	Ash
	(~2½ cigs.)	(~22 cigs.)		
Smokers' ash	21	207	24 ± 1 8*	26 ± 0 9
Smokers ash (remeasured)	19	189	22 ± 1 3	25 ± 0 9
Smoking machine	23	239	28 ± 2 1	33 ± 1 2
Smoking machine	21	201	25 ± 0 8	28 ± 0 4
Condensate from 300 cigarettes	≯ 0 35		≯ 6 µg	

* Errors given as standard deviations.

It may be concluded, therefore, that such radioactivity as is present in cigarette tobacco remains in the ash and that very little, if any, is transferred to the smoke. If the figure of 6 µg is taken as representing the maximum radioactivity (as potassium) which could appear in the smoke of one cigarette, the highest radiation dose in the lung would be produced if this amount lodged as one particle. Such a particle, however, would be some 300 µ in diameter and would deliver a dose-rate to cells adjacent to it of the order of 2–3 mr per week. This is approximately equal to the dose rate which body tissues receive continually from their average potassium content, local gamma rays, and cosmic rays.[12] For smaller particles the dose rates would be reduced directly as the particle diameter (since the specific radioactivity of the material is constant) and would, therefore, be much less than the natural background dose rate. Where tumours have been known to be due to radioactive materials lodged in the body, the dose rates involved were at least 10,000 times greater than the levels considered here.[13]

The measured activity of the ash per cigarette appears to be rather higher than that of the tobacco, although the differences are hardly outside experimental error. Separate tests showed that the discrepancy was not due to the ash from the cigarette paper. It might be accounted for, however, by the average radioactivity of the air which is usually such that the filtering of a few litres of air by the cigarette could increase the radioactivity of the ash by amounts of the order observed.

Department of Medical Physics and
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University of Leeds

F W SPIERS
R D PASSEY

INTUSSUSCEPTION

SIR,—I would like to comment on your leading article[1] and the letter by Mr Jones and his colleagues[2] in Newcastle.

Acute intussusception must always be associated with pain, which varies in intensity with the type of intussusception. The pallor of the associated shock may be the only evidence of this at the time when the child is being examined. A tumour can be palpated if examined for carefully enough in every case, although an anæsthetic may be necessary to bring about sufficient relaxation of the abdominal wall to enable the mass to be felt. A bimanual examination with one finger in the rectum may help in making a diagnosis.

The duration of the symptoms before treatment is commenced is admittedly a very important factor, both in estimating the prognosis and in deciding on the best method of treatment. It is not the duration of the trouble, however, that should decide the question of operation, for one occasionally sees patients where an intussusception has been present for several days, but, because of the extreme mobility of the ileocæcal region, in some of these cases, the intussusceptum does not become strangulated and the intussusception may be reduced by hydrostatic pressure. Usually, when an intussusception has been reduced in this way, the fact that complete reduction has occurred can be readily determined—and without the help of radiography. This is due to the fact that in most cases, after reduction, some of the enema passes through the ileocæcal sphincter into the small bowel, and causes an even distension of the abdomen, the degree of distension depending on the time occupied in holding in the bowel the saline or fluid used. On palpating such an abdomen, the fact that there is a considerable quantity of fluid in the small bowel can be readily appreciated, especially because, before the enema is given, the abdomen is usually soft and flaccid. If additional help is required in diagnosing complete reduction, it can be obtained by measuring the circumference of the abdomen before and after the giving of the enema. In those cases where none of the fluid passes into the small bowel, even though the intussusception has been reduced, there will be no distension, and an operation should follow.

Mr Jones and his colleagues say that the majority of cases reported by me as having been reduced by hydrostatic pressure were admitted to hospital within twenty four hours of the onset of the intussusception. This statement, while literally true, implies that the success of reduction by hydrostatic pressure in my series was due to early recognition and treatment. I feel sure that the majority of cases, reported by anyone, anywhere, first come under observation by a surgeon or are admitted to hospital in the first twenty four hours after the onset of the trouble. In 30 of the 100 consecutive cases reported[3] in 1926, the intussusception had been present for twenty four hours or more, and there was no death in any case where the intussusception had been pres[illegible] for less than forty eight hours. Another series[4] of a showed the same proportion admitted to hospital · twenty four hours—namely 15, Several of these : reduced by hydrostatic pressure where the duration e intussusception had been several days, and 1 which been wrongly diagnosed as prolapse of the rectum led quite readily to hydrostatic pressure after seven ʟ.

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[12] Spiers, F W Burch P R J Biological Hazards of Atomic Energy Oxford 1952 p 203

[13] Spiers F W Brit. J Radiol 1953 26 296

[1] *Lancet* 1953 i 229

[2] Jones J D T, Hindmarsh D Court S D M Jackson, R B *Ibid* p 392

[3] Hipsley, P L *Med J Aust* 1926, ii 201

[4] Hipsley P L *Ibid*, Nov 9, 1918

every case of intussusception is operated on, then ast 45% will be operated on unnecessarily No one ay with certainty that the opening of the abdomen young infant is devoid of risk Now that we have a iod whereby complete reduction by hydrostatic ure can be diagnosed in the majority of cases there ld appear to be no excuse for operating on every case.

dney Australia. P L HIPSLEY

VISITING CHILDREN IN HOSPITAL

ʀ —I was agreeably surprised to read the annotation his subject in your issue of Nov 28 This the more t was in one of my early writings that attention first drawn to the detailed facts of the hospitalisation ma as described in your opening sentence

ossibly because of the emergencies of war time, my inal monograph [1] attracted no great public attention . I have reason to believe however, that there were r and more pertinent reasons for its non acceptance ook some years before the evidence I had marshalled accepted in psychiatric circles: more resistance eared from one's general medical colleagues some of m even today do not believe in ' the hospitalisation ma. (A prominent member of a regional board nly denied its existence and his remarks received e publicity)

consider, therefore that the *Ministry of Health* were precipitate in their action in attempting to impose y visiting on recalcitrant, or at any rate unbelieving pital staffs. I think a good deal of educational work needed first to bring about what has been called "attitude of acceptance." Otherwise the hostility ly engendered between doting parents and a sceptical sing staff can nullify all the benefits of the visiting elieve that Sir James Spence had somewhat similar eriences when he first brought in the mothers to e their own small babies in his hospital at Newcastle l that by suitable education (of both sides) the iculties were smoothed out

Visiting children in hospital is sure to cause emotional nes at times—in the parent or the child or both—and ess the nursing staff are suitably warned and prepared luding an explanation of why all the upheaval should necessary the outcome in its own way may be every as bad as no visiting at all

eeds. H EDELSTON

SIGN OF ASCITES

Sir,—I would like to draw attention to a hitherto described sign for the detection of free fluid in the itoneal sac, which I have been employing with vantage, since 1948

The patient lies on his back with his legs partly flexed; flank is then flicked or percussed with the firm stroke of a ger while the opposite flank is auscultated with a Bowles al piece and stethoscope. Normally it is customary to r only one sound with each percussion stroke but in the e of ascites, with moderate or large amounts of fluid one en hears a reduplicated sound or even two distinct sounds.

In my experience the double sound is about 6–8 es as common in cases of ascites than with other causes abdominal enlargement. I therefore recommend this a confirmatory diagnostic sign of free fluid in the itoneal sac

Bombay India. RUSTOM JAL VAKIL.

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[1] Edelston, H, Separation Anxiety in Young Children A Study of Hospital Cases. Genetic Psychology Monographs, 1943.

CORONARY HEART-DISEASE AND PHYSICAL ACTIVITY OF WORK

SIR —In an earlier letter [1] I indicated that in my opinion physical idleness was a *factor* in the production of degenerative changes in the coronary arteries Since this was published in 1951 there have been two statistical inquiries which have given some support to this theory First, there was the article by Dr Logan [2] who stated that his findings tended to support my theory and a similar view put forward by Dr Stocks.[3] Second, there is the elaborate investigation by Dr Morris and his colleagues described in your issues of Nov 21 and 28

I think it is a pity that Dr Morris and his colleagues took for their inquiry occupations in which the exercise difference is relatively slight I suggested in 1951 that a comparison should be made between scholastic teachers and physical training instructors. There may be statistical difficulties about this, but I still think that it should throw light on the problem

I have been convinced on this matter for some time, as a result of personal observation but I am certain that the only statistical way to convince the doubters—and until the recent articles appeared I have found hardly any support—is to study some special group in which the incidence of coronary artery disease is high and to show that amongst the group there is a special subgroup which has a low incidence and an exercise factor very much higher than that of the main group I have tried to do this myself but without financial and other support it is very difficult nowadays to undertake an inquiry of this kind I thought that the Swiss and Austrian guides would be good subjects for investigation and I made some efforts there but the idea of their dying of coronary-artery disease was treated with such hilarity that the matter could not be pursued

I have for some years been trying to find support from the pathological side by trying to get detailed *personal histories of the type of life which has been led* in cases which I have examined post mortem and by attempting to relate these to the condition of the coronary arteries. Owing to smallness of numbers and the difficulty of getting accurate histories these have not proved conclusive but I am persisting Meanwhile although I cannot be certain of the following statements, I believe that they contain some of the keys to the problem

(1) A few people are so genetically constituted that their coronary arteries are resistant to all adverse factors.

(2) In the remainder the principal factors are of a simple mechanical nature (*a*) the bigger the coronary arteries, the more room there is to have atheromatous plaques without disastrous results (*b*) the faster the blood goes through the coronary arteries the less likely it is that they will develop obstructions in their walls.

(3) Assuming these statements to be correct then the part played by exercise is clear The more you exercise the bigger your coronary arteries the more you exercise the faster the blood flows through them and the more difficult it is for an obstruction to develop on the walls.

(4) I think that the exercise, to be really effective as a protector of the coronary arteries, must be fairly vigorous. The round of golf once a week is not much use

It is probably worth while directing the type of exercise to attempt to maintain a good tone of the abdominal muscles Vigorous contraction of the abdominal muscles must have some effect on the blood flow in the coronary arteries Possibly the success of clamping the aorta during attempts at resuscitation may be related to this factor

I have for some time been considering various exercises with a view to providing the optimum coronary protec tion I think skipping is the best, but people are intolerant of it and, for the ordinary person, dancing of the Scottish country type is the most practicable proposition

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[1] *Lancet* 1951 i ,87
[2] Logan, W P D *Ibid* 1952 i 758.
[3] Stocks, P *Ibid*, 1951 i, 351

Two final points the most magnificent coronary arteries, related to age, I have ever seen were in a man who died recently under an anæsthetic and had an advanced degree of stenosis of the aortic valve, and I wonder why the incidence is so much lower in women

Houston,
Renfrewshire

EDGAR RENTOUL

DIAGNOSIS OF CARBON-MONOXIDE POISONING

SIR,—The alveolar air of patients with carbon-monoxide poisoning contains a small percentage of CO, according to the equilibrium [1]

$$P_{co} = \frac{HbCO\,(P_{O_2} + 300\,P_{co})}{300}$$

where HbCO is the percentage of carboxyhæmoglobin in the blood and P_{co} and P_{O_2} are the partial pressures of CO and O_2 in the alveolar air For example, 16% HbCO gives 1 part per 10,000 of CO

A method of estimating such traces of CO in air quite simply and accurately has been developed,[2] using palladosulphite in silica gel Air is sucked through tubes containing this material by means of a double aspirator which gives the correct rate of flow A respiratory attachment suitable for obtaining an equilibrium sample of alveolar air has been designed for use with this instrument

This method can be carried out by a semi skilled person in three minutes and appears to offer some advantages in clinical diagnosis compared with spectrometric or titrimetric tests on the patient's blood

Such rough tests as I have made encourage me to think that this method would be effective in diagnosis, but more experience is needed

London N W 3

L T MINCHIN

A CONSULTATION FEE?

SIR,—Would a shilling per consultation, either as an alternative to or as an addition to the shilling per prescription, benefit the community as a whole?

It would in the first place reduce the cost of the health service, which so far has been an embarrassment to both post-war party governments It might discourage some of the "is-your visit really necessary" patients from growing like perennials in general practitioners' waiting rooms It would free these overworked benefactors from attending to numerous minor complaints and so enable them to spend more time on the cases that need their care

Indirect benefits to the community resulting from this would include a greater proportion of the population retaining confidence in their own ability to lead healthy lives, less wear and tear on general practitioners and their wives, and consequently on their families and households, and less prescriptions being asked for and therefore less medicines being prescribed, but greater counter sales at the chemists of first aid dressings, simple household remedies, and dietary accessories The cost of the latter would then be transferred from the nation's to the individual's pocket, while the main costs of diagnosis, of treatment, and of ethical medicines would continue to be borne by the National Health Service

The collection of this second "bob" is a domestic affair, the difficulties of which might be outweighed by the advantages gained A shilling per consultation, as well as a shilling per prescription, would have the serious disadvantage that it would impose further financial burdens on those who depend on medical treatment for their health (and therefore for their happiness), and also on those who, with large families, are the first to feel the pinch caused by increases in the cost of living But a shilling per consultation instead of a shilling per prescription has decided advantages Although this point was the subject of debate in the earlier days of the health service, the years of experience that have since intervened may have thrown different light on the subject It would be interesting to hear the reactions of those whom such a change would concern the most

Woldingham, Surrey

RAYMOND L HANBURY

TRAUMATIC RUPTURE OF THE BILE-DUCTS

SIR,—The comprehensive review of this rare abdominal injury given by Mr Milnes Walker (Nov 7) prompts me to give details of a case at the Royal Hospital, Wolverhampton, 16 months ago According to Mr Milnes Walker's record, it would be the fourth reported since 1938 and the fifty second in the literature

The patient, a young, fit, intelligent man of 21, was injured in a motor cycle accident on June 16, 1952

On admission to hospital he was shocked, and had a compound fracture of the right tibia and fractures of the right patella and right femoral shaft He improved considerably with resuscitation, but 2–3 hours after the accident he began to complain of pain in the upper right abdomen. There was tenderness in the right hypochondrium, and localised rigidity, with normal liver dullness There was no sign of bruising in this area, though it was clear that the right side of his body had received the main force of the impact Catheterisation showed a clear urine It seemed probable that there was injury to one of the organs in the right upper quadrant, probably the liver It was decided, therefore, to explore the abdomen, while the orthopædic surgeon, Mr E A. Freeman, would deal with the fractures at the same time, when the abdominal condition became clear

Laparotomy—There was a small quantity of thin bile-stained fluid in the abdomen and gross œdema and infiltration of bile in the free margin of the lesser omentum and in the region of the common bile duct There was also a small tear of the under surface of the liver which was hardly oozing any blood at all Careful exploration of the bile stained tissues established the following points

(1) At the upper end of the bile stained tissues there was a small opening from which bile trickled, and a probe, passed through this, travelled towards the liver in the right hepatic duct, but attempts to pass it into the cystic duct, which appeared just above the opening, showed that this was torn longitudinally for about $^1/_2$ in

(2) From the posterior lip of the opening a thin strap of bile stained duct lining extended down behind the duodenum, presumably the posterior wall of the common duct

(3) The lower margin of the duct had retracted behind the duodenum

The lesion, therefore, seemed to be an incomplete tear of the common duct extending to the cystic duct, with wide separation of the ends, attenuation of the connecting segment, and considerable collapse of the lumen

These factors made insertion of a tube difficult and stricture formation likely, while the split in the cystic duct excluded cholecystoduodenostomy as an alternative The words of Rutherford Morison on the subject of rupture of the urethra seemed apt "unless your skill can prevent the development of a stricture, you are presiding at the opening of a lifelong tragedy" So Mr R L Benison, consulting surgeon to the hospital, was called in to help to avoid such a tragedy

A rubber T tube, which had to be small enough to enter the collapsed lumen, was inserted with some difficulty, and sutures, which similarly had to be few in number because of the small calibre of the duct, were inserted over the tube Periductal drainage was established and the abdominal wall sutured

The fractures were treated at the same time, and chemotherapy was started

Postoperative Course—There was some distension and sickness during the first 4 days, but a normally coloured stool was passed Jaundice then appeared, the stools became clay-coloured and bile drained freely but in diminishing quantities, for the next 18-19 days.

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[1] Henderson Y Haggard, H W Noxious Gases. New York, 1943 p 165

[2] Methods for the Detection of Toxic Gases in Industry no 7 Carbon Monoxide H.M Stationery Office, 1950 See Minchin *Iron & Steel Lond.* September 1953. p 425

Cholangiography on the 23rd postoperative day showed most of the dye around the tube but a little had passed into the duodenum. The tube was then gradually clamped over a week, and then kept continuously closed for 3 days with no ill effects except a little local discomfort Further cholangiography showed that the dye passed into the bowel The tube was removed on the 30th day

The patient has been quite well ever since as far as his abdomen is concerned The fractures required prolonged rehabilitation but he is now fit for light work.

The outstanding features of the case were:

(1) The extreme collapse of the common bile-duct rendering anatomical identification in the bile-soaked tissues difficult.

(2) The involvement of the commencement of the cystic duct in the tear, which excluded the use of this duct as an alternative bile channel by means of a cholecystenterostomy

(3) The relatively smooth convalescence without as yet, 10 months later, symptoms of stricture formation, which would usually be expected within a year if this was going to be a troublesome development.

(4) The laceration on the under-surface of the liver which suggests that the force may have been in such a line as to cause the liver to crush or tear the ducts against the vertebræ—a mechanism suggested by Lewis.[1]

My thanks are due to Mr R L. Benison for permission to publish these notes and for his help with the operation.

Wolverhampton, **HENRY B YOUNG**

'CHEMOTHERAPEUTIC AGENT' AND 'ANTIBIOTIC'

SIR,—The purpose of my letter (Oct. 17) was to expose the implications and possible consequences which could arise from Dr Erwin's suggested "basis for 'a more exact liberal definition of chemotherapeutic agent'" (Oct. 24) His more recent use of an 'exact liberal definition' clearly vindicates my point No-one would regard aspirin as an antibiotic simply because 'a sufficient quantity destroys the life of man." All would, without *exception, and unhesitatingly, regard it as a* poison and this quite apart from the fact that 'antibiotics' act, as Professor Waksman (Aug 22) has said "in dilute solution to destroy micro-organisms.

Terms, Sir have connotations—they imply the attributes while denoting the subject If 'chemotherapeutic agent' and antibiotic are as Dr Erwin declares 'terms recently coined, and therefore, still evolving, Dr Erwin can scarce forbear to cheer the sanity and wisdom of Professor Waksman's sober summary 'Proper definitions are available without sacrificing historical perspective, scientific accuracy or current usage, and this should not be left to the whim of individuals who decide to redefine important terms according to their own points of view"

Cape Town. **M GLASS**

CIRCUMCISION

SIR,—In the literature on this subject and in the excellent article by 'Sir Daniel Whiddon" (Aug 15) no mention is made of the fact that it is possible in normal persons, *without* any operation to obtain the same end result—namely an exposed glans The method is as follows:

> During the year or so before puberty the boy is told to retract his foreskin and clean the glans every time he takes a bath. Gradually as puberty approaches, and as the glans becomes hardened the foreskin is kept retracted. This has the effect of *allowing* the glans to grow *through* the foreskin, leaving it behind The end result is a penis indistinguishable from, or superior to the most skilfully circumcised one.

Instruction in this procedure appears to be usually passed from father to son in certain families; few doctors seem to have heard of it There is possibly some risk of balanitis, and the manœuvre should therefore be carried out preferably only under the intelligent supervision of the father

UNCIRCUMCISED

DEXTRAN SULPHATE

SIR,—We should like to answer Dr Berenbaum's comments (Nov 28) on a statement in our paper reporting the therapeutic trial of dextran sulphate One patient (case 8) died from coronary thrombosis while under treatment The statement that staining with toluidine-blue of histological sections taken at necropsy failed to show storage of dextran sulphate is held to be a possible misinterpretation since it is suggested that this method of demonstrating polysaccharides is unreliable unless the material is protein bound or otherwise rendered insoluble

In the first place while we would agree that toluidine blue is an unreliable stain for *neutral* polysaccharides, since in fact *it fails to stain them, in our hands it has been found capable* of demonstrating by the metachromatic reaction concentrations as low as 1-2 μg of *highly sulphated* polysaccharides (such as the material used in our clinical trial)

Secondly during the preliminary biological screening of dextran sulphate we have had available material from animals given dextran sulphates of various molecular sizes Comparisons have been made of tissues prepared by freeze drying techniques, by fixation mounting and staining in alcohol and by the ordinary histological routine after treatment with fixatives containing mercuric salts or with formol saline. It has been our experience that when material was demonstrable by either of the first two methods, it was also demonstrable by the use of the usual techniques in material fixed in watery fixatives.

Experimental evidence from animal studies suggests that while protein binding is essential for the *uptake* of sulphated polysaccharides by the reticulo-endothelial cells it is not essential for the demonstration of these compounds in the cell For example, it has been shown that dextran sulphates of large molecular size form insoluble complexes with the plasma proteins and that these particulate precipitates are cleared from the blood-stream by the phagocytic activity of reticulo endothelial cells Material staining metachromatically with toluidine blue is demonstrable as granules within these cells where it persists for twenty eight days or longer[1] Examination of these granules in freeze-dried material in the ultraviolet light microscope and measurement of the absorption at a wave length of 2800A° gave no indication of the presence of protein in the phagocytosed material if the animal had been allowed to survive longer than four hours after the injection of the dextran sulphate This suggested that the protein moiety of the phagocytosed material was split off and *metabolised quickly by the active proteolytic enzymes* known to be present in reticulo-endothelial cells, leaving the sulphated polysaccharide component to undergo slower katabolism[2] This is in keeping with the findings of Kaplan et al[3] and of Coons et al.[4] who showed that even heterologous and foreign proteins disappear considerably more quickly from reticulo-endothelial cells *than similarly phagocytosed polysaccharides*

On the other hand it has been shown that dextran sulphate of uniformly small molecular size (such as that used in the clinical trial) does not form insoluble complexes with the plasma proteins In our opinion it is for this reason that even in much greater dosage than that used clinically the injection of such material does *not result in the appearance of granular metachromatic* material in the reticulo-endothelial cells of experimental nimals[3] From the results of similar investigation of he material from case 8 (the only human material so ar available), it appeared to us that a similar situation revailed.

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[1] Lewis K, M *Ann. Surg* 1935 102 237

[1] Walton, K. W *Proc. R. Soc. Med.* 1951 44 563

[2] Walton K. W *Brit J Pharmacol.* (in the press)

[3] Kaplan, M. H Coons, A H. Deane H W *J exp Med.* 1950 91 15

[4] Coons, A H. Leduc E H. Kaplan M. H *Ibid*, 1951 93 173

It is perhaps worth mentioning that the sulphation of lextran interferes with its staining by the periodic-acid chiff technique (presumably by blockage of glycol roups), so that the technique of Mowry and Millican[5] s, in any case, inapplicable for use in the investigation f these compounds Further investigation of the distri ution of dextran sulphate is now being undertaken by adio autography using dextran sulphate labelled with adioactive sulphur (S^{35})

Department of Experimental Pathology
University of Birmingham. KENNETH WALTON,

Medical Research Council Industrial
Injuries and Burns Research Unit,
Birmingham Accident Hospital. COLIN RICKETTS

A J.H.M.O APPOINTMENT

SIR,—The letter from "S.H.M.O" in your issue of)ct 24, which was concerned with the S.H.M.O vis à-vis he consultant, prompts me to describe an experience f mine as a J.H.M.O vis-à-vis the S.H.M.O.

Some time ago I accepted a post as J.H.M.O at a small ıospital The only other doctor at the hospital, the medical uperintendent, was a consultant

When I had been at the hospital some months it came to ny notice that my predecessor as assistant medical officer, man with the same qualifications and experience as myself, ad been a senior registrar, and that he had left when the egional board decided to abolish such a grade at the hospital During his stay there the actual "establishment" had been ne consultant, one senior registrar, and one J.H.M.O., though here had never been a J.H.M.O at the hospital before my rrival. The regional board, when they decided to abolish he senior registrar grading, amended the establishment to e one consultant, one S.H.M.O., and one J.H.M.O My predecessor had been offered the S.H.M.O grading shortly before his departure and had refused it The S.H.M.O post was not advertised before my arrival or during my tenure of the J.H.M.O post

With this information in my head, I told the superintendent that in my view there seemed to be at least a reasonable case for my applying for S.H.M.O status. He agreed that there was in the ordinary sense of the words, but added first, that the regional board would never upgrade a J.H.M.O to S.H.M.O status in a hospital and leave him in that hospital, and second, that if I approached the board on the ground that I was doing the work of one J.H.M.O plus at least that of half a S.H.M.O., they might well see fit to advertise the S.H.M.O vacancy In that case, the superintendent said, someone other than myself might be appointed to the vacant S.H.M.O *post and although there would then still be room on the* establishment for a J.H.M.O., the board might think the hospital could function perfectly well with just two doctors, as heretofore In other words, I should be sacked.

I swallowed hard at this, and in consequence of it and of certain other allied irritations, took steps to obtain a post outside the N.H.S as soon as I could When I announced my imminent departure, the superintendent said that there was really too much work at the hospital for two doctors, and every effort would be made to replace me by a S.H.M.O *and* a J.H.M.O (He also, I should add, expressed great regret that I should be "leaving him"—as he put it) Shortly after I left the hospital, I met a S.H.M.O from the same region He had the same qualifications and experience as myself, and he told me that he had recently been upgraded to S.H.M.O status while remaining in the hospital at which he had previously enjoyed J.H.M.O status. I brought this to the attention of my old superintendent, who maintained a dignified silence

To complete the story soon after my entering the hospital as a J.H.M.O., my superintendent took a month's holiday, leaving me in charge I took his place, while a locum took mine The person who obtained the locum appointment therefore had less responsibility than I during that month At the same time she received (in salary plus emoluments) a rate of remuneration considerably in excess of my own I continued to draw J.H.M.O's salary for the month during which I did a consultant's work. Officially the superintende of another nearby hospital "deputised" for my absent chief in fact he visited the hospital *for just ten minutes* during th month my chief was away—ten fruitless minutes at that

Accordingly, when the superintendent threw cold wa on my idea of applying for S.H.M.O. status, I answered tha I would not deputise for him during any future holiday I had reached this decision, I said, *de facto* because of treatment I was receiving in the matter of my grading *de jure* because it is clearly laid down that J.H.M.O.s ar officers who ... have less responsibility than other hospita officers of non consultant status. I could hardly therefore I said to my superintendent, deputise for a consultant in conscience I should be *going above my station of life* He sighed as a colleague, and submitted as an employee the board At intervals subsequently he hinted that the had come for him to have a holiday On each occasion I agreed —and asked whom he had *in mind* as his temporary deputy I hinted that, as I should presumably be the senior resident medical officer during his absence, I should not feel perfectly confident if his deputy were to visit the hospital at a rate o two and a half minutes a week My superintendent took no holidays.

The following points are noteworthy

1 That, a senior and a junior post being vacant, only the junior post was advertised.

2. That the doctor appointed was expected to assume pa or all of the duties of the vacant senior post as well as hi own.

3 That when he suggested he might at least apply for the senior post, he was threatened with the possibility of losing the junior post

4. That he was told that a certain principle obtained in making appointments to such senior posts only to discove very much later that such a principle did not in fact obtain

5 That a junior doctor was called upon to deputise for a very senior doctor during the latter's holiday, while pure paper arrangements were made for another very senior doctor to deputise and no effort was being made to fill a vacant senior post

EX-J.H.M.O.

BARBITURATES AND ALCOHOL

SIR,—Your annotation of Sept. 12 led me to bring together some observations made during the war, and more recently Fig 1 shows the blood barbiturate levels of a normal person who was on two occasions given amylobarbitone ('Amytal') 0·4 g orally on an empty stomach. Fig 2 shows the blood-barbiturate levels of a proved cirrhotic with an alcoholic history who was given amylobarbitone 0 2 g. orally on an empty stomach Comparison of the two figures shows that while the ratio of the dose to the peak blood level reached is not significantly higher in fig 2 than in fig 1a or b the peak is prolonged in the patient with established liver damage.

In fig 3 the lower curve represents blood galactose levels in a normal person given galactose 40 g. when fasting The test was carried out in the morning after 24 hours' abstention from alcohol The upper curve represents the corresponding levels in the same person the morning after an evening when an excess—but not

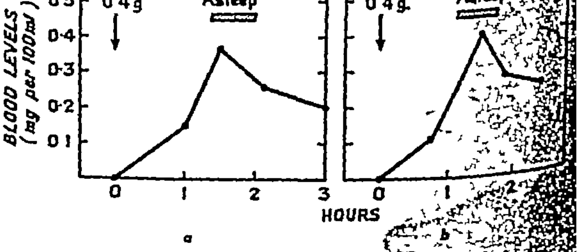

Fig. I.

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5 , R. W., Millican, R. C *Amer J Path* 1953, 29 523.

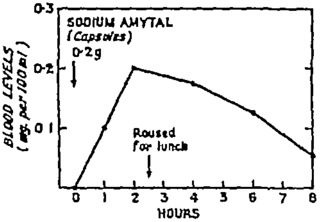

Fig 2.

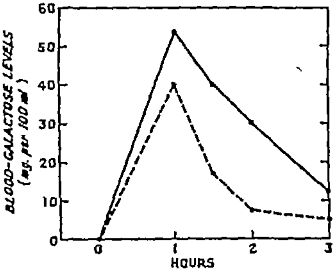

Fig. 3

a vulgar excess—of alcohol had been taken I am doubtful whether taken by itself, the second curve would be regarded as proof of liver dysfunction; but in conjunction with the control curve it strongly suggests that the alcoholic excess had reduced the efficiency (temporarily at any rate) of this person's liver Viewed together the two sets of data help to explain why it may be dangerous to take barbiturates after taking any substantial dose of alcohol or if one's way of life involves regular consumption of spirits

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NICHOLAS MARTIN

SURGICAL EMERGENCIES

SIR,—Today when hospital planning and hospital staffing are being widely discussed, and when operating theatres and extensions are being built or are due to be built it seems opportune to discuss the merits of a surgical urgency unit Urgent surgical cases constitute almost half the surgical admissions in the average general hospital, and such a unit would greatly improve their treatment.

These cases coming into hospital throughout the twenty four hours of the day are often kept waiting This may be caused by general list cases blocking the general surgical theatres. Preoperative treatment, transfusions &c., are frequently done under difficulties in a crowded ward. At night, semi-darkness in the ward and a diminished nursing staff accentuate the difficulties.

There is a strong case for having an urgency unit attached to the main general hospital of each group The unit should be controlled by a whole time consultant surgeon (If acute orthopædic surgery is worthy of a whole-time consultant, acute general surgery is too) The consultant should always be available for advice in diagnosis, and treat difficult cases himself The duty registrar and house-surgeon from the duty surgical unit would work under him, treating the casualties and general surgical emergencies

The urgency unit should have 5–10 male and female beds, and its own theatre, sterilising anæsthetic and preparation rooms. Surgical emergencies probably requiring operation would be admitted to the unit. These cases may include all instances of open trauma and abdominal urgencies. The patients would be prepared for operation operated on, and retained in the unit until 9 A.M. the following day when if fit to be moved they would be sent to the appropriate ward whose turn it was to receive urgencies or sent home Very few urgencies are too ill to move in bed in hospital The aftercare of the urgent cases would be the responsibility of the whole time urgency surgeon with the coöperation of the surgeon in charge of the ward to which the patient is sent Head injuries would be admitted to the unit and treated by the surgeon or neurosurgeon as deemed advisable Orthopædic emergencies—i e., compound fractures—would be treated by the orthopædic staff and only admitted to the urgency unit by special arrangement Obviously local arrangements would be necessary to suit individual hospitals.

The urgency unit has the following advantages

1 It enables urgent surgical cases to be prepared for operation or resuscitated with the maximum of convenience and the greatest efficiency and without undue delay All transfusion outfits and preoperative apparatus, &c., can be made instantly available and used in good lighting By concentrating all surgical urgencies in one department there can be economy in instruments, nursing, and technical personnel

2 The general surgical wards can have better and smoother working conditions, and they suffer less disturbance; this is especially valuable during the night

3 The theatres serving surgical wards can be used more fully and with a more regular routine as they are not required for urgencies

The principle of concentrating the treatment of urgent surgical cases would amply repay the public and the National Health Service. Besides the advantages outlined above, the care, foresight, and experience of the established surgeon at present almost limited to the treatment of "list" cases, would be available for the urgent cases which constitute 40–50% of surgical admissions to general hospitals.

Advantage, too should be taken of our resources of adequately trained surgeons (100–150 fifth year surgical senior registrars [1]) to staff these units. Increased opportunity would be available for further research into acute surgical disease, which is still responsible for the premature loss of thousands of lives annually

Withington Hospital,
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N F KIRKMAN

SOMATOTROPHIC HORMONE AND THE PANCREAS

SIR,—Recent reports have emphasised the possibility that the islets of the pancreas may play a part in the processes of growth. It has been suggested that the peripheral effects on growth of the pituitary somatotrophic hormone (S.T.H.) may be brought about, partly or wholly, by the liberation from the islets of insulin and/or glucagon, produced respectively by the B and A cells [2–5] In this connection, we have been carrying out some morphological studies on the islets of animals under S.T.H. treatment.

In the first experiment, two groups of intact rats, weighing 105 ± 2 g were treated for two to ten days with corticotrophin (A.C.T.H. Armour) or S.T.H. (Armour) the daily dose varying from 1 to 10 mg; nine hours before sacrificing they were given colchicine (40 μg per 100 g body weight). Histological examination of the pancreas stained by Gomori's chromohæmatoxylin phloxyn method showed a large number of atypical mitoses in the islets in both groups but in the S.T.H. treated group the absolute number of mitoses and the proportion of dividing A cells was much higher than in the A.C.T.H. treated group

In another experiment a strain of mice with hereditary pituitary dwarfism, due to recessive anterior pituitary hypoplasia, was used. It was observed that the islets of dwarfs in comparison with those of normal animals of the same strain, were very rich in A cells and consisted of hypotrophic

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1 Walton J N., Forrester R. M. *Brit. med J* 1953 i, suppl. 156
2. Bornstein, J Reid, E. Young F G *Nature Lond.* 1951 168 903.
3. Best, C. H *Diabetes* 1952, 1 267
4 Elrick, H. *Proc. Soc. exp Biol., N Y* 1953 82, 76.
5. Young F G *Abstr int. Congr Physiol. Montreal,* 1953 p 18

A and B cells After giving S T H for several weeks, the islets of the dwarf animals increased in number and size and the A and B cells became hypertrophic, whereas the A/B cell ratio was hardly changed at all

Our observations suggest that there is a close relationship between S T H and the pancreatic islets On morphological grounds it seems very probable that this pituitary hormone could stimulate both types of cell in the islets, producing insulin and glucagon But further work is needed to decide whether S T H acts on the islets directly or indirectly and how far the peripheral effects of this hormone can be attributed to stimulation of the islet cells

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CESARE CAVALLERO

BACT COLI IN THE CAUSATION OF INFANTILE DIARRHŒA

SIR,—In recent years many reports[1-6] have appeared about the rôle of *Bacterium coli* type O, 111 B, 4 and type O, 55 B, 5 in infantile diarrhœa, and there is already much evidence to incriminate these organisms

In a previous letter,[7] we described the examination of *Bact coli* O, 111 B, 4 and O, 55 B, 5 in the stools of healthy infants and of those suffering from non-epidemic infantile diarrhœa We have also investigated two outbreaks of infantile diarrhœa, associated with *Bact coli* O, 55 B, 5, in a home for infants—that is, in an enclosed environment (apart from new admissions)—here in Nagoya

Fæces from each child at the home were examined weekly, from June 25, 1952, to March 1, 1953, and more frequently when cases of diarrhœa occurred *Bact coli* types O, 111 B, 4 and O, 55 B, 5 were looked for routinely and, from October, 1952, O, 26 B, 6 as well

In July and November, diarrhœa, associated with *Bact coli* O, 55 B, 5, was present in two outbreaks In the first outbreak, 10 out of 20 children were involved This strain was isolated from 7 of them The onset was comparatively mild and signs were very slight In the second outbreak, out of 18 children, 15 were ill and the strain was isolated from 13 of them. This outbreak began very suddenly, there was 1 death, and 3 cases were severe, 6 moderate, and 5 mild Thus, in the two outbreaks, there were 25 cases, of which 20 yielded this strain of *Bact coli*, no other pathogenic organisms were isolated

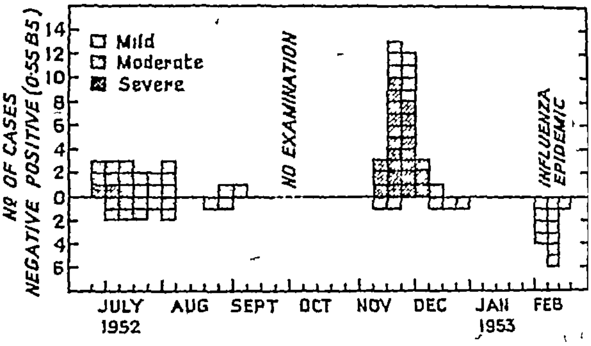
During the period of the outbreaks 5 infants were discharged and 3 were admitted, so that out of the 18 exposed to the second infection, 15 had been exposed to the first If a large number of susceptible infants had entered the home after the end of the first outbreak, this might have accounted for the increased severity of the second attack, but in fact only 3 were admitted, and some of those who were severely ill in the second outbreak had been exposed to the first

The organism was isolated between one and six days before the clinical onset in 6 of the bacteriologically proven cases After clinical signs had subsided and treatment had been stopped, this organism reappeared in 10 out of the 20 cases, but the strain usually disappeared in about a month

In the child who died in the second outbreak, the onset was mild but on the fifth day there was a sudden rise in temperature, accompanied by meteorism, restlessness, and cyanosis and finally by convulsions and death within fourteen hours In this case there were many *Bact coli O, 55 B, 5* in the large intestine and terminal ileum None were isolated from the other organs The intestine was moderately inflamed but the most serious change was fatty degeneration of the liver

In agglutination tests in the other cases there was usually a temporary rise between the second and sixth weeks

Bacteriological investigations of the stomach contents (6 cases), pharyngeal swabs (6), vomit (4), and blood (1) were all negative



Two outbreaks of infantile diarrhœa in a home for infants in Nagoya

During the second outbreak 4 adults (2 doctors, a nurse and a laundress) were found positive for *Bact coli* O, 55 B, 5 2 of them had nausea, abdominal pain, and some diarrhœa.

In the infants' home, two months after the second outbreak, there was an influenza epidemic On this occasion, there were 8 children with diarrhœa Bacteriological examinations were made regularly, but the stools were all negative

Chloramphenicol was given in 7 cases, aureomycin in 3, and streptomycin in 2 We found that all three drugs were effective, but in the 2 cases given streptomycin, there were slight relapses on the sixth and fifteenth days of the illness.

In November, 1952, we tried to obtain these strains in another infants' home in which 60 infants lived Cultural examinations were performed once a week for a month in all the children, but there were no positive results

From these results, it seems clear that these outbreaks of infantile diarrhœa were closely connected with *Bact. coli* O, 55 B, 5 The following facts are interesting

(1) There were 4 children who had diarrhœa with *Bact. coli* O, 55 B, 5 in the first outbreak and who also carried this strain in the second

(2) In the two outbreaks, the severity of the clinical signs and the epidemiological features were different.

TOHRU OGAWA
Professor of microbiology
JIRO OGAWA
Nagoya City University, Japan. Professor of pædiatrics.

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[1] Braun O H., Aust B *Mschr Kinderheilk* 1953 101 75
[2] Kirby A C Hall E G Coackley W *Lancet* 1950 ii, 201
[3] Kropler P Zischka W *Z Kinderheilk.* 1953 72 625
[4] Rogers K B *J Hyg, Camb* 1951 49 140
[5] Wright J., Villanueva, R. *Ibid*, 1953 51 39
[6] See leading article *Lancet* 1952, ii 323
[7] 953 i, 602

INTUSSUSCEPTION IN AN ADULT

SIR,—Teasdale has lately reviewed[1] the literature concerning colo colic intussusception in adults, pointing out that this condition is not as rare as such a review might suggest In 1911 Eliot and Corscaden[2] collected 300 cases, of which only 20 were due to carcinoma, but in Teasdale's series of 242 cases of carcinoma of the colon, seen during the past twelve months, 11 presented with intussusception

I should like to describe a further case

A woman, aged 71, was admitted to hospital as a case of intestinal obstruction on Dec 24, 1950 She had had hæmatemesis 12 years ago, and a partial gastrectomy for duodenal ulcer 6 years ago She had been well until 2 days prior to admission For the past 48 hours she had had severe generalised colicky abdominal pain which had kept her awake at night with one small vomit on the first day of the attack Her bowels had opened regularly until the day of admission. There had been no blood or mucus in the stools

She was a pale and wasted old lady Her tongue was coated and furred There was no distension or tenderness in the abdomen, but a hard sausage shaped mass was felt in the left hypochondrium

At laparotomy on the night of admission, using a right lower paramedian incision, a loose colo colic intussusception was readily reduced from the left hypochondrium. There was no interference with blood supply The cause was a large fungating carcinoma of the cæcum, about 2 in in diameter There were enlarged glands in the mesocolon and mesentery, but no evidence of distant spread Her general condition seemed satisfactory and there was little evidence of dilatation in the small gut, so a right hemicolectomy and end-to-end anastomosis were performed The wound was closed without drainage

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[1] Teasdale, D H *Brit J Surg* 1953, 41 128
[2] Eliot, E Corscaden J A *Ann Surg* 1911, 53, 169

Section of the tumour showed a tubular columnar-celled carcinoma of the cæcum Sinus catarrh œdema, and congestion but no evidence of secondary carcinoma in lymphatic gland from mesocolon

The patient made a surprisingly good recovery and the postoperative convalescence was uneventful She was discharged as an inpatient on Jan. 11 1951 -

Hackney Hospital,
London E.9

R F READ

SUBCLINICAL POLIOMYELITIS INFECTIONS

SIR,—Your leading article of Nov 14 has already been criticised by Dr Bradley (Nov 28) for its misuse of Melnick and Ledinko's [1] interesting study of the development of antibodies in the sera of children during an epidemic in 1948 in Winston-Salem North Carolina There are, however a few points to be added and two misconceptions appearing in your article should be corrected

First it is worth looking at the figures more carefully The epidemic showed an incidence of 62 cases per 100 000 population (highest national figure for this country 20 per 100 000) the ratio of paralytic to non paralytic cases was high (2 : 1) and the *calculated* incidence of actual cases per subclinical infection varied from 6 to 16 per 1000 according to the age group of the children studied (before 1947 the incidence was probably somewhere about 1 per 1000 in this country) By the end of this severe epidemic the percentage of children studied who were immune to each of the three types of virus were

(a) In the upper economic groups

Type I	Type II	Type III
23 (10)	30 (19)	23 (23)

(b) In the lower economic groups

Type I	Type II	Type III
66 (38)	58 (43)	46 (45)

(The numbers in parentheses show the percentage figures before the epidemic.)

Unlike you Sir, I find these figures intensely depressing Winston-Salem had not only had a severe epidemic in 1948 it had also had an epidemic in 1944 and all three types of virus had been represented in one or other epidemic. Yet, even excluding new entrants by birth over half the child population was still susceptible to one or more types of the virus At this rate severe epidemics can go on almost indefinitely—as in fact they have done for the last 50 years in the United States of America.

This brings me to the correction of the first of your two false assumptions. You assume that evidence of subclinical immunisation by poliomyelitis *viruses* is incompatible with evidence that poliomyelitis *disease* runs along narrow streams of the population and that one must therefore choose one set of evidence and reject the other You choose to reject the narrow streams.'

But both sets of evidence are incontrovertible, and no conception of the epidemiology of poliomyelitis which does not accommodate both is admissible. Fortunately they are easily reconciled if one recognises the possibility that different strains of the three viruses may differ—like many other pathogenic organisms—in their virulence. Thus the narrow streams of *disease* are caused by the virulent strains carrying a high rate of clinical disease and the wider *subclinical infection by milder strains* carrying a much lower rate An analogy with *gravis* and *mitis* strains in diphtheria is obvious; both these strains produce a common immunity but they vary markedly in the amount and severity of disease which they cause in the process. Since variations of virulence of strains of poliomyelitis virus are a common laboratory experience, there is nothing revolutionary in suggesting that the same phenomenon is at work during epidemics of poliomyelitis

The severity of any particular epidemic will therefore depend on

(1) the proportion of virulent and non virulent *strains spreading through the population; and*

(2) the population's 'immunological state' (in other words its previous experience of strains of the prevalent types of poliomyelitis virus) To quote two examples In an epidemic among Eskimos in Chesterfield Inlet [2,3] the incidence was as high as 1 in 5 (5%, of the *total population* died and 14% became paralysed) while incidences as low as less than 1 in 1000 have been reported for other population groups.[4-6]

The Eskimos of Chesterfield Inlet were presumably exposed to unusually virulent strains of a type of virus to which they had not previously been exposed (adults were as susceptible as children) Something similar to the Eskimo experience but fortunately not as severe, was seen among British Servicemen in Malta in the winter *of 1942-43* [7] *Their susceptibility to an epidemic affecting* the Maltese children (82% were under 5 years old) contrasted strongly with the immunity of the Maltese adults, who although there was no history of previous *epidemics* in the island were virtually immune Clearly the virulence of strains of a type familiar to the Maltese but not to the British had increased *and with it the ratio of clinical to subclinical infection* Thus exposes your second false assumption—that there is a universal constant ratio for clinical and subclinical infections, which led you to apply the findings in Winston Salem arbitrarily to this country The ratio varies not only from *population to* population but *also for the same* population from year to year

In fact a conception of strains of different virulence within the three different immunogenic types of poliomyelitis viruses makes easy sense of a lot of apparently conflicting data, and yet, since it conforms with general epidemiological principles does not strain the imagination Its immediate practical application is, of course, to the control of the spread of the disease. A strain which has caused one clinical case is for that very reason to be regarded as a dangerous strain which if allowed to spread is likely to show a high incidence of clinical disease (cf the epidemic in Rye last year) Its spread should therefore be prevented by every means we have The mild strains responsible for the subclinical infection we neither could nor would prevent from spreading—in fact, if we could we would help them as much as we would hinder the others, since it is important that they should infect, and so immunise, as many persons as possible before the more virulent strains can infect and not only immunise but also paralyse many of them The present non intervention policy which you would appear to favour results only too often in the race being won by the virulent strains. The result is a steady rise in notification figures all over the world.

In conclusion two recent confirmations of the validity of the 'narrow streams' of disease must be mentioned since your article questions this obvious fact

1 In New York [8] the incidence of clinical cases among household contacts of cases was found to be 40 times higher than among controls. Further 93% of the secondary cases occurred within two weeks of the initial case

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[1] Melnick, J L., Ledinko N *Amer J Hyg* 1953 58 207

[2] Adamson J D Moody J P Peart, A. F W., Smillie, R. A., Wilt, J C. Wood, W J *Canad med. Ass. J* 1949 61 339

[3] Paul, J R., Riordan J T., Melnick, J L. *Amer J Hyg* 1951 54 275

[4] Turner T B., Young L. E., Maxwell, E S. *Ibid* 1945 42 119

[5] Turner T B, Hollander D H., Buckley S., Kokko, U Pentti, Winsor C. P *Ibid*, 1950 52 323

[6] Casey A. E. Fishbein W I., Schabel, F M. jun. Smith, H. T *Amer J publ. Hlth* 1950 40 1241

[7] Seddon, H. J., Agius, T, Bernstein H. G G Tunbridge, R. E. *Quart. J Med.* 1945 14 1

[8] Siegel, M., Greenberg M. *New Engl. J Med.* 1953 249 171

2 In the much misquoted epidemic in Denmark at least 28% of the cases studied were found to have a history of contact with another actual case—indirect contacts do not appear to have been studied [9]

The matter is urgent and we cannot afford the luxury of prejudice and ill informed "opinions" Compared with others this country has been fortunate in its experience of poliomyelitis, but we must not abuse our good fortune The experiences of Denmark, Sweden, Canada, and the United States of America, to mention only a few countries, in recent years may well be ours next year unless we initiate deliberately *in advance* measures which will otherwise be *forced upon us—but too late* For "if restrictive control measures in a population are to exert a significant influence they should be applied early in an outbreak to the adults and children who are familial and non familial contacts of the frank case" [10] This was the conclusion of workers studying the distribution of virus and conforms with epidemiological experience not only of poliomyelitis but of many other epidemic diseases

Wingfield Morris Orthopædic
Hospital, Oxford

MARGARET AGERHOLM

CORTISONE AND RHEUMATOID ARTHRITIS

SIR,—I should like to give support to the letter by Dr Renshaw (Nov 28) on this subject, for I have found an extract of intestinal mucosa most beneficial in a variety of rheumatic cases seen in general practice over the past six or seven years

Looking over some fifty or sixty cases, including rheumatoid arthritis, osteo-arthritis, spondylitis deformans, gout, and fibrositis, one is impressed by the fact that in only one case was no improvement registered Failure in this case was, I believe, due to the fact that the patient failed to continue the treatment as instructed, she has since had a variety of other treatments with no benefit

The improvement in general health of these patients is most impressive and is followed gradually by diminished pain and increased mobility of the joints

An extract of erepsin, when injected into the tender areas in cases of fibrositis, has a remarkable effect, after an initial stiffness, lasting twenty four to thirty six hours, all pain goes

In practice the treatment is easy to give and control with a minimum of time and trouble, there being no necessity to see patients more frequently than once every four to six weeks

I am quite certain that, if patients can be persuaded to carry out the treatment properly, they will slowly but steadily improve

Sheringham Norfolk.

H C GELDARD

SIR,—I have been in charge of a rheumatism clinic at Warrington Infirmary, in conjunction with the orthopædic clinic, for 27 years Because of the large number of rheumatoid arthritis cases attending, which congested the other work of the physiotherapy department, I endeavoured to relieve the pressure on the department by giving other forms of treatment for this disease These included gold, vaccines, deoxycortone and vitamin C, 'Irgapyrin,' and phenylbutazone (by injection and by mouth)

About eight years ago, after consultation with Dr Arnold Renshaw and on his advice, I decided to give a trial to treatment of a series of cases by intestinal extract, with a balanced protein diet

Given an intelligent and cooperative patient with the requisite amount of patience during the initial few months of this treatment, definite improvement has occurred and has been maintained in well over 100 cases, with less striking improvement in many others Crippled housewives have been able to do their housework and previously disabled industrial workers have returned to modified work

It is important to realise that some considerable time—varying with the individual patient—must elapse before improvement commences In these patients sedatives have been discouraged as much as possible In the few young patients I have treated, the results were very good. The general health in nearly every case was improved and weight increased in debilitated patients

Grappenhall,
near Warrington

BERNARD MURPHY

MARROW BIOPSY

SIR,—It seems to me that a simple and efficient method of performing bone-marrow trephine biopsies is an essential requirement for a hæmatology department. The examination of bone marrow smears, invaluable as it is, does seem, not too infrequently, to need the complementary histological examination of both bone marrow and its adjacent bone The reasons are well known and have been noted by Custer [1] and Block [2] In particular, histological examination is necessary to obtain a reliable guide to the nature and extent of the non-cellular and non-hæmopoietic tissue structures [3] and to the presence of abnormalities such as foci of metastatic neoplasm or granulomata [4-6] Furthermore, the relation of the hæmopoietic to the non hæmopoietic tissues is probably better seen in sections, simple smears sometimes being misleading owing to either blood dilution [1, 2] or greater resistance to suction removal of the more primitive hæmopoietic tissues [7] and sometimes the megakaryocytes.[8] This different resistance to suction removal is particularly important because it results in selected smears which are not representative of the true quantitative and qualitative structure of the marrow [9, 10] This defect may be especially troublesome when dealing with patients who are either taking drugs which depress hæmopoiesis or who have diseases such as erythræmia [11] or chronic myeloid leukæmia [12] in which the hæmopoietic tissues sometimes appear to differentiate into a non hæmopoietic phase

Of course, the examination of bone marrow sections has its drawbacks, one being the difficulty sometimes encountered in identifying the various hæmopoietic cells and another the procedures involved in obtaining the specimen for histological examination Such procedures vary from the simple ones of sectioning fragments of needle aspirated marrow [13] or using needle-like trephines of about no 17 B W G [14, 15] to the more *complicated methods* using ordinary 1 cm diameter trephines [14] or excising $^1/_2$–1 in segments of rib [17] Unfortunately, most of the simpler methods are either inefficient or yield too small a specimen, the more complicated ones seem too drastic for day-to day use in a hæmatology department

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[9] See *Brit med. J* Oct. 31 1953 p 991

[10] Pearson H E Rendtorff R C *Amer J Hyg* 1945 41 1 ' 179, Pearson H E Braun, G C Rendtorff R C, [illegible] G M, Frances, T Jun. *Ibid* p 188

[1] Custer, R. P An Atlas of the Blood and Bone-marrow Philadelphia and London, 1949

[2] Block M. *Illinois med J* 1950 98, 202

[3] Block M Jacobson L O *J Amer med Ass* 1950, 143, 1390

[4] Görmsen H *Acta med scand* 1948 131 154

[5] Weisberger A Heinle R. *Amer J med Sci* 1949, 217, 263.

[6] Stahel R *Folia Hæmat, Lpz* 1939 61 345

[7] Block M Jacobson L O *Acta hæmat* 1948 1, 165

[8] Berman L Axelrod, A. R., Kumbe, B S *Amer J clin. Path.* 1948 18 898

[9] Dameshek W Henstell H H, Valentine, E H *Ann. intern Med* 1934 11 801

[10] Weisberger A Heinle R *Amer J med Sci.* 1949 217 1,7

[11] Marson F G Meynell, M J *Brit med J* 1953, 1, 1113

[12] Black Schaffer B, Stoddard, L D *Amer J Path* 1953, 29, 413

[13] White J C Baker, J R Griffin, J G *J Path. Bact* 1946, 58 155

[14] Turkel H Bethel F H *J Lab clin Med* 1943, 28, 1246.

[15] Bernstock L Sterndale H *J clin Path* 1951, 4, 378.

[16] Custer R. P *Amer J med Sci.* 1933 185, 617

[17] Hutt M S R. Smith, P, Clark, A. E, Pinniger, J L. *J clin Path.* 1952 5 216

Dameshek[15] has described a less drastic plan using a slightly modified Seyfarth's 5 mm. diameter trephine.[16] It seems, therefore, that this size of trephine has a valuable place in hæmatological investigations and it is of interest to note that there is readily available in this country a very suitable trephine for this type of biopsy. This instrument is the trephine for the Blackburn skull traction appliance; it has a T-shaped handle, an adjustable guard allowing a maximum penetration depth of about 8 mm., and an adjustable central pin which aids in rapidly ejecting the excised bone fragment into the fixative. It cuts out a bone fragment of 4 mm. diameter.

With this instrument the biopsy is rapidly performed. Using full aseptic precautions and with the patient under general anæsthesia, the skin over the selected bone is incised for a distance of 2 cm.; the skin is retracted, the periosteum incised, and, if possible, the edges of the periosteum stripped up with a Watson-Cheyne dissector. With its central pin retracted and the guard set at the appropriate depth, the trephine is then rotated into the bone and gently rocked to break the deep trabeculæ and the bone fragment removed within the trephine cavity. An assistant transfers the bone fragment to the fixative. If the bone is unduly sclerotic and does not readily break away, the fragment may be forced out of the bone with a 4 mm. Jenkins gouge. The marrow adjacent to the trephined hole is scraped out with a meibomian-cyst scoop and reserved for smearing. If bleeding is troublesome the bone cavity is filled with a freshly prepared solution of Maw's thrombin, and the periosteum replaced but not sutured; on occasions it may be advantageous to pack the cavity with thrombin-soaked gelatin sponge. On no account should the cavity be packed with surgical gauze. Two sutures are placed in the skin and the wound covered with a dry dressing. Although I have not yet done so, both Custer[14] and Dameshek[15] perform their trephine biopsies under local anæsthesia.

I am much indebted to Mr W. Parke, F.R.C.S., who first suggested to me the use of this trephine. The trephine may be obtained from the London Splint Co. Ltd., 60 Weymouth Street, London, W.1, and the 4 mm. Jenkins gouge and the large meibomian-cyst scoop may be obtained from Messrs. Allen & Hanburys Ltd., London.

London, S.W.3 A. B. HILL.

ALL IN THE DAY'S WORK

SIR,—The Widdicombe discussion (Nov. 14 and 28) on the performance of simple clinical pathology in general practice seems to me, as a hospital pathologist, to be eminently sensible. I do agree that a simple method of hæmoglobin estimation would be best, especially if one observer were to use such a method constantly. One minor criticism refers to the method of syringe sterilisation. Baking is obviously far better than boiling for syringes, as for most joints of meat; but to use an ordinary domestic oven several precautions must be taken. Few are provided with thermometers, and these do not necessarily record the temperature of the part of the oven which might be used for sterilisation. Thermostatic controls are fitted to most of them, but once more they only control the temperature in one part of the oven. Experience has shown me that quite wide variations may take place elsewhere in the oven and it may have quite marked 'hot spots' and 'cold spots.' It is to obviate these, of course, that special design of laboratory ovens is necessary. The same remarks apply to domestic refrigerators, as is well known to anybody who has tried to store blood in one. Note, in addition, that needles used in taking capillary blood must be kept in Lysol.

One final comment is that although it is a bad pathologist who insists that his findings must be 'right,' it is also a bad clinician who insists they must be 'wrong.' The results of laboratory tests are facts which cannot be overlooked any more than such clinical signs as a cardiac murmur or a palpable spleen. In many cases there are anomalous findings, although an ideal picture of what is happening would account for them all. A laboratory result which does not fit the diagnosis has not necessarily been produced by faulty technique. We may not know what it means and it may not help us immediately, but it may well be a clue to further discoveries.

Department of Pathology,
Royal Liverpool Children's Hospital. R. E. REWELL.

Parliament

Air Pollution

IN the House of Commons on Dec. 2 Mr MACMILLAN, Minister of Housing and Local Government, said that the Government had considered the interim report of the Committee on Air Pollution.[1] On Nov. 17, before the report was submitted, doctors were authorised to prescribe masks under the National Health Service for patients suffering from heart or lung disease living or working in an area where smoke-polluted fog is likely to occur. Following the committee's recommendations, the Government had already arranged for the Meteorological Office to issue warnings when serious fog was expected to prevail for at least 24 hours in areas of normally high pollution. These fog warnings would be accompanied by advice to the public about the ways in which they could help to reduce smog and its ill effects. The Government were studying further steps which might be taken to ensure application of these measures and make them more effective while awaiting the next report of the Beaver Committee.

QUESTION TIME

Use of Agene in Flour

Replying in the House of Lords to Lord HANKEY, Viscount WOOLTON, Chancellor of the Duchy of Lancaster, said that although good progress had been made, the investigators into the use of agene in flour for human or animal consumption were not yet complete. It was hoped, however, that it would be possible to make a statement on the subject within the next three months or so.

B C G Inoculation of School-leavers

Mr S. P. VIANT asked the Minister of Health whether any means had been devised to follow the medical history of school-leavers who underwent B.C.G. inoculation; and how, should such persons subsequently develop tuberculosis, can the fact that they had been inoculated be ascertained in the case of those who left the area in which the inoculations were performed.—Mr IAIN MACLEOD replied: Local health authorities have already been advised to keep records of the vaccination of older school-children together with information of their follow-up. These records should enable the date of a particular inoculation to be ascertained later by communication between the authorities concerned.

Tuberculosis Notifications

In answer to a question Mr MACLEOD stated that the tuberculosis notifications for England and Wales for 1952 numbered 48,093 (respiratory 41,904; other forms 6189). He regretted that these figures had been inadvertently omitted from table 37 of the *Annual Abstract of Statistics*.

Medical Grading of National Service Recruits

Replying to a question Mr HAROLD WATKINSON, parliamentary secretary to the Ministry of Labour and National Service, stated that since 1948 the numbers of men called up for National Service and the numbers rejected on medical grounds were as follows:

Year	*Called up*	*Rejected on medical grounds*
1948	150 900	27 750
1949	166 000	36 370
1950	174,200	47,314
1951	168 651	43 866
1952	170,384	47,899

Sexual Offences

Replying to a question Sir DAVID MAXWELL FYFE, the Home Secretary, said that in 1938 the number of unnatural offences known to the police in England and Wales was 134; the number of attempts to commit unnatural offences (including indecent assaults on male persons and cases of importuning for immoral purposes dealt with on indictment) was 822, and the number of offences of gross indecency was 320 The corresponding figures for 1952 were 670, 3087, and 1686

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[14] (see earlier page)

[15] Dameshek, W. Amer. J. med. Sci. 1935, 190, 617.

[16] Seyfarth, C. Dtsch. med. Wschr. 1923, 49, 180.

[1] The report is summarised on p. 1257.

Sir Robert Boothby Is the Home Secretary satisfied that the law relating to sexual offences is really effective and workable? Is he satisfied with the present institutional treatment of sexual offenders, and does he not think that further research into the problem, perhaps beyond purely departmental research, is urgently required? Sir David Maxwell Fyfe One element in dealing with this matter is the protective element in punishment, because homosexuals in general are exhibitionists and proselytisers, and are a danger to others, especially the young, and so long as I am Home Secretary I shall give no countenance to the view that they should not be prevented from being such a danger As regards treatment, I should like to assure the House that we are very much alive to the problem in our prisons today Arrangements are made for medical attention, especially of a psychiatric kind But the difficulty in these cases is that for treatment to be successful there must be coöperation, and in many cases coöperation is refused

The third point that must always be borne in mind is that apart from the true invert, there are homosexuals who use that instead of ordinary sexual intercourse, the male prostitutes who come up on these importuning cases, and the sensationalists who would try any form of excitement and indulgence These three types of cases, apart from the male invert, can be dealt with, and are being dealt with, by our prison system I am trying to study and give my careful attention to the whole problem, but it would be wrong not to stress these points

Mrs Braddock Will the Home Secretary consider carefully the medical aspect, because many magistrates who understand the situation are reluctant to give terms of imprisonment in these cases because of overcrowding in prisons where men are put two or three in a cell? It is considered that sending them to prison accentuates the trouble rather than cures it Sir David Maxwell Fyfe Unfortunately, owing to the shortage of space, there are about 5000 people who are three in a cell This matter has been carefully examined, and I believe that the chances of increasing homosexual inclinations from that cause have been greatly exaggerated Although, of course, homosexuality exists in prisons—as Sir Alexander Paterson said, you cannot help it in a "monastery of men unwilling to be monks"—I think the effect has been exaggerated We have not been able to find any evidence of much increase of inclination

Examination of Mentally Deficient Children

Mr A J Irvine asked the Home Secretary whether, in cases where a child was examined under the procedure referred to in section 9 of the Mental Deficiency Act, 1913, it was the practice of his department to permit, if the child's parents desired it and at their own expense an examination of the child by an independent medical expert of the parent's choice and to give consideration to the report following such examination —Sir David Maxwell Fyfe replied Section 9 of the Mental Deficiency Act, 1913, empowers me to order the transfer to a suitable institution, or the placing under guardianship, of a child detained in an approved school or, in certain circumstances, in a remand home, if I am satisfied from the certificates of two qualified medical practitioners that the child is a defective Such certificates are considered most carefully, in the light of the medical advice available to the Home Office, before any action is taken on them. I am prepared to give favourable consideration to requests by parents for an examination by a doctor of their own choice where there is reason to think that the further opinion would be of value in the few cases where such requests have been made hitherto it has not been considered that a further examination would serve any useful purpose

Medical and Dental Recruitment

Mr Percy Morris asked the Minister of Health how far he was satisfied with the rate of recruitment to the medical and dental professions, and how far he anticipated that the needs of local government social services would be adequately met from such sources during the next three years —Miss P Hornsby Smith replied Recruitment in the medical and dental profession is through entry into university medical and dental schools—which are outside the Minister of Health's control He has no grounds for thinking that the number of doctors qualifying will be insufficient to provide for recruitment to local government or other services but fears that the shortage of dentists will not be overcome in the period mentioned

Fluoridation of Water-supplies

Replying to a question Mr Macleod said that the Government had decided to accept the recommendations of the report of the United Kingdom Mission which studied the fluoridation of domestic water supplies in North America as a means of controlling dental caries In conjunction with the Minister of Housing and Local Government, who was responsible for public water supplies in England and Wales, the Secretary of State for Scotland and he proposed to arrange for studies to be made in some selected communities of the various aspects of the fluoridation of water supplies before considering whether fluoridation should be generally adopted in this country An approach would be made to certain local authorities to invite their coöperation in making these studies

Woodberry Down Health Centre

Colonel Malcolm Stoddart Scott asked the Minister what information he had about the extent to which the Woodberry Down Health Centre, Stoke Newington, was being used, and what accommodation at the clinic was still unused Miss Hornsby Smith replied The whole of the centre is in use except two dental laboratories, one dental surgery, a medical store, a clinical side room, and the doctor's night-duty accommodation

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Obituary

THOMAS YULE FINLAY

M.D Edin., F R C.P E

Dr T Y Finlay died on Nov 28, in Edinburgh where he had spent his whole professional life and where he was the first maternity and child-welfare medical officer

Born in Paris in 1882 of Scottish parents, his early days were spent there, but when his family returned to Edinburgh he became a pupil at the Royal High School and then proceeded to the university where he graduated M.B in 1907, obtaining the M D with high commendation in 1912 His brother-in-law, Dr Gaston Variot, of Paris, was a pioneer in the infant-welfare movement, and Finlay early in his career showed a keen interest in child care This interest was also encouraged by his intimate association during his hospital residencies with the late J W Ballantyne and John Thomson Finlay always acknowledged the great debt he owed to these two distinguished men

In 1913, when he was medical superintendent of one of the large poorhouses in Edinburgh, he introduced new methods of treatment, supervision, and record-keeping of the children resident there which attracted the favourable attention of the Local Government Board for Scotland In 1919 he was the natural choice of Edinburgh Corporation as medical officer in charge of the newly formed maternity and child-welfare section of the public-health department He was blessed with the gift of bringing happily together voluntary and official agencies for the care of mothers and young children, and the section of which he was head expanded its functions steadily and achieved fruitful results

In 1922 he took the M.R C P E, and the same year he became an assistant physician at the Royal Hospital for Sick Children He was also appointed senior assistant physician to the reorganised children's unit of the municipal hospitals' service He was a lecturer and examiner on diseases of children and child hygiene at the university and at many other teaching bodies in the city, and he was early in the field in the training of health visitors He became F R.C P E in 1927 He was a member of many medical and pædiatric societies. An honour which he greatly valued was that of honorary membership of the British Pædiatric Society, of which he was an original member When he retired under the age-limit in 1947 his faithful services to the city were publicly acknowledged In his retirement he flung himself wholeheartedly into the work of several of the voluntary organisations with which he had been closely associated during his official career

He is survived by his wife, daughter, and two sons.

Notes and News

LIBRARY OF THE ROYAL COLLEGE OF PHYSICIANS

The first published catalogue of the library of the Royal College of Physicians of London which appeared in 1660, contained 1278 titles Today the college has 40 000 printed books, 600 manuscripts, a small collection of letters and the H. M Barlow collection of bookplates from medical institutions. The Harveian Librarian has lately issued a short introductory note which sets out some of the library's story

The original collection was based on the library of Thomas Linacre, who founded the college in 1518 William Harvey was another benefactor who gave not only books but a museum in which to house them A great deal was lost in the Great Fire of 1666 but the bequest of the Marquis of Dorchester's library in 1688 did much to offset this catastrophe The most notable gift of recent years has been Dr Lloyd Roberts's library received in 1921—an addition of considerable value to medical historians. The library is now very well provided with biographies and has over 5000 engraved portraits and photographs of medical men But its shelves have never been restricted solely to medical works: its treasures include the Wilton Psalter (c 1250) Caxton's *Recuyell* (c. 1475), and the only known copy of the first book on dancing (Paris c. 1488)

MEDICAL WAR RELIEF FUND

The committee of this fund, at a meeting in London on Nov 17 approved a report prepared by the distribution subcommittee on the year 1952–53 The report showed that 41 awards amounting to £2000 had been made. The largest gift (£500) was to the Australian War Relief Fund which was in need of help to deal with urgent cases. As in previous years, educational grants were in the majority and 15 widows were helped with the payment of school or university fees or the purchase of school outfits. At Aug 31 the balance remaining in the fund was just over £13,000

THE ST JOHN AMBULANCE AIRBORNE

The St John Ambulance Brigade can now provide attendants for patients travelling by British European Airways and it is hoped to extend this service to other air lines in due course The members of the service have passed airworthiness tests and are qualified in air duties and emergency midwifery as well as in first aid and nursing The service is voluntary but patients will be expected to pay the attendant's fare and reasonable out-of pocket expenses. Further particulars may be had from brigade headquarters, 8, Grosvenor Crescent, London S W 1

LINEAR ACCELERATOR AT ST BARTHOLOMEW'S HOSPITAL

St. Bartholomew's Hospital London, is to have a linear accelerator producing X rays by bombardment of platinum foil with electrons of a potential of 15 million volts. This will be the largest apparatus of its sort in existence for medical purposes A similar machine is being built for Harwell for physical research. At the hospital the apparatus will be used for the treatment of cancer the development of new methods of treatment, and fundamental research on the effects of high energy on the human body The cost is being met by the governors from their endowed funds and King Edward's Hospital Fund for London have promised a contribution.

STRESS AND ATHEROSCLEROSIS

To test a clinical impression, the frequency of atherosclerosis and some other degenerative conditions, as the cause of death, was compared in two Jewish groups in Denmark.[1] The one group, long established in the country and affluent but dwindling in numbers was believed to have led a more sheltered life and consumed a diet richer in cholesterol than the second group composed of immigrants from Russia who had had a hard struggle to establish themselves. So far as stress was concerned, it could not be maintained that the men of the two groups differed greatly, though their different economic status exposed them to superficially different physical and emotional demands. Between the women of the two groups however there were conspicuous differences in respect of such presumptive stresses as marriage childbirth and domestic work. Corresponding differences were not found in the total proportion of deaths from atherosclerosis but the age of death from this cause was earlier in the immigrant group of women The authors do not carry out any statistical analysis beyond the calculation of percentages, and it is difficult to draw any firm conclusions from their findings. The two populations studied were small and there were many possible sources of error nevertheless the report is an interesting essay in social medicine.

W V S HOSTELS FOR MOTHERS AND CHILDREN

The hostel which was opened by the Women's Voluntary Services in 1945 at Clapham, to help mothers and babies suffering hardship as a result of the war has now been moved to Streatham. It is intended to help women who have no home of their own and who have nowhere to go before or after discharge from hospital A resident matron and two assistants teach the mothers to look after their babies and give instruction on the principles of feeding and babies laundering and so forth.

The W V.S also run a short-stay home at Whitstable where children can go whose mothers have been taken into hospital or who might break down if they did not have a rest away from home At Aldeburgh they run a recuperative home where children may stay for a month convalescing from chest diseases. Further particulars may be had from the W V.S 41 Tothill Street, London S W 1

NEW FILMSTRIPS

Four filmstrips recently produced for the World Health Organisation set out to inform the public of some of its activities.[1] *Penicillin*, which is perhaps the best of them, deals mainly with the way in which it is being used to combat endemic syphilis bejel, yaws, and pinta. *The Fight against Tuberculosis* shows some of the aetiological factors and gives an account of the work carried out at the Tuberculosis Centre Istanbul *Malaria* uses an anti malaria campaign in Thailand as an illustration of what preventive measures can do *For Babies Born too Soon* shows developments in the care of premature infants. In the first three the over-all picture is fairly well balanced, but this last one seems to emphasise unduly the work of a single clinic in Paris A fifth filmstrip[2] has been prepared to teach teen-agers and young wives the methods and value of breast-feeding The value of all these filmstrips will depend largely on the ability of the lecturer who uses them. None of them make any serious attempt to exploit the visual medium, and few of the pictures are more than a background illustration.

University of Cambridge

On Nov 28 the degree of M.D was conferred on M G Thorne and J K. Wagstaff.

University of London

The degrees of M B B.S, have been awarded to D D J Rees.

University of Manchester

The following have passed the final examination for the degrees of M B, CH B

Sheila Berry J K Bleasdale, Cyril Booth Margaret A Broughton J W Chamberlain, G H. H. Dwyer Pauline R. Dyckhoff Gerald Gold Lawrence Goldie Aubrey Greenbaum Mabel L. Haigh Daphne J Hall Fred Heyworth John Johnson J R. Jones, L K Levens, J S. Lord, F G Lucas, Jean McCracken Clifford Mawdsley V B Maxwell F W Murphy W C. Newport, Jeffrey Parkin Lawrence Reece Eve M. Roper J G D Russell Ruth M Sellars Joan R. Singleton, J N Standring A O F Stuart A T Thompson S T Whitehead.

University of Dublin

On Dec. 3 at the School of Physic Trinity College the following degrees were conferred:

M.D —E. W Lillie.

M B B Ch., B A O.—Stanley Allen, I C. Bailey, Anne Bewley A. W Browne, William Brownlees, Barbara M. Cooke William Dobson, Frank Fine, Dorothy A Foster J B Gill, Henry Hartman N L. Harris, C. A. Isola, Ariwodo Kalunta, J E Latham, G R. L. Lyons, Donald McCaughan, S. W McVicker J R. Noble James O'Carroll, W G Speer J D Tate, E. C Tees, K. G Weyhausen

L.Med —L. A H Oulton.

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[1] Physical and Mental Stress and Consequential Development of Atherosclerosis within the Jewish Population of Denmark. By GRETHE HARTMANN and FINI SCHULSINGER. Copenhagen Rosenkilde & Bagger 1953 Pp 78 Dan. Kr 8 00.

[1] Penicillin A weapon against disease Cat. no. U 58 15 frames The Fight against Tuberculosis. Cat. no. U 56 50 frames. Malaria. Cat. no. U 57 51 frames. For Babies Born too Soon Cat. no U 54 19 frames. All monochrome 1952. Produced for the World Health Organisation and available from Unicorn Head Visual Aids Ltd. Broadway Chambers, 40 Broadway Westminster, London, S.W 1

[2] The Nursing Couple Cat. no. U 55 Colour 20 frames, 1952 Produced by the Central Council for Health Education and available from Unicorn Head Visual Aids Ltd.

Royal College of Physicians of London

Dr J T Ingram will deliver the Watson Smith lecture on Monday, Jan 11, at 5 P.M, at the college, Pall Mall East, S W 1, on the Significance and Management of Psoriasis.

Royal College of Surgeons of England

On Monday, Dec 14, at 5 P.M, at the college, Lincoln's Inn Fields, London, W C 2, Prof Geoffrey Hadfield will deliver the Kettle lecture He will speak on the Dormant Cancer Cell

Industrial Injuries Advisory Council

Prof R E Lane, F R C.P, has been reappointed to this council, and Mr A Miller, F R.C.S E, and Dr L 'G Norman have been appointed

Collecting Tissue Grafts

The French Académie de Médecine (*Times*, Dec 4) is seeking to introduce legislation to permit surgeons to take tissue grafts from the bodies of young people killed in road accidents.

Chartered Society of "Queen Square"

The council of this society will shortly hold an election to fill vacant pensions (£20 per annum) which are available for people with incurable nervous diseases Forms of application and further particulars may be had from the secretary of the society, National Hospital, Queen Square, London, W C 1

Heberden Society's Dinner

Speaking at the Royal College of Surgeons on Dec 4, Sir David Maxwell Fyfe said that as Home Secretary he was interested to find that Heberden had been one of the first debunkers of the "super-poisoner" For thousands of years people had feared the master poisoner, who made the flower kill through its perfume or the ring through its touch, but Heberden had let in the cold air of science, describing these stories as the idle results of ignorance and superstition Heberden had also been well versed in the classics—before the days when the Greek dramatists had become no more than a quarry for Viennese psychologists seeking names for their complexes This year the Heberden oration had been given by Sir Russell Brain, and the Heberden round had been conducted in Lancashire by Dr J H Kellgren, who had since been appointed professor at Manchester Paying tribute to Heberden as a physician of the past, Sir David also paid tribute to a physician of the present—one, he said, who does not stand austerely on a pinnacle of fame but gives his friendship to an infinite variety of people who don't deserve it, and thereby enriches their lives. Lord Horder, in reply, somewhat reluctantly forgave the Home Secretary for these personal remarks after all, Sir David might not have a chance of making them again—he might not be asked again. Welcoming Prof R E Tunbridge as his successor in the presidency, he said that the society had had a successful year With a membership limited to 100, it had a waiting list of men and women well versed in what he must now regretfully call rheumatology Comparing the position of the subject now with its position twenty years ago, it was evident that Cinderella had now been found by the Prince and taken to the dance The three major advances of the last two decades came from recognising (1) that chronic rheumatism was a hotchpotch which needed separation both technically and administratively, (2) that it was not a local or a focal disease but an expression of the patient's fitness or otherwise and (3) that the nervous system, in its relation to the vertebral column, played an important part in many cases of rheumatism This had been well illustrated in the Heberden oration on Spondylitis delivered by Sir Russell Brain, to whom Lord Horder proceeded to present the Heberden medal Dr W S C Copeman proposed The Guests in varying blends of respect and disrespect, and drew an equally light hearted response from Miss Patricia Hornsby Smith, parliamentary secretary to the Ministry of Health

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CORRIGENDUM *The Anæsthetist's Responsibility*—In the third paragraph of this leading article (Nov 21, p 1080) the third sentence should read "Perhaps the most helpful measure is the administration by inhalation of a broncho dilator such as isoprenaline, and postural drainage with vibratory and clapping percussion of the chest" In the fifth paragraph the last word in the sixth line should be "synchronous"

Mr Patrick Clarkson is to be the guest speaker at the annual meeting in January in Chicago and Cleveland of the American Society Hand Surgery

Diary of the Week

DEC 13 TO 19

Monday, 14th

Royal College of Surgeons Lincoln's Inn Fields W C 2
5 P.M *Prof Geoffrey Hadfield The Dormant Cancer Cell* (Kettle lecture)
Postgraduate Medical School of London, Ducane Road, W 12
4 P.M Dr Brian Ackner Emotional Factors in Treatment Response
University College, Gower Street, W C 1
4 45 P.M Mr H Gutfreund, PH D Molecular Forces in Protein Solutions (Last of two lectures)
Royal Eye Hospital St George's Circus, S E 1
5 15 P.M Dr T H Whittington Accommodation Clinically Considered, Cycloplegics, Retinoscopy
Medical Society of London, 11 Chandos Street, W 1
8 30 P.M Mr John Bunyan, L.D.S Application of the Microscope to Medicine Dr George Lumb Pathology and Spread of Cancer of Breast. Dr W H. McMenemey Degenerative Changes in Brain Following Stoppage of Heart During Surgical Operation

Tuesday, 15th

Royal College of Surgeons
3 45 P.M Mr C le Q Darcel Comparative Pathology of Leukotic Conditions in Man and Fowl (Imperial Cancer Research Fund lecture)
5 P.M Mr D Innes Williams Chronically Dilated Ureter (Hunterian lecture)
Institute of Dermatology, St. John's Hospital, Lisle Street W C 2
5 30 P.M Dr F Ray Bettley Atopy
West End Hospital for Nervous Diseases, 40, Marylebone Lane, W 1
5 30 P.M Dr T Rowland Hill Neurological demonstration.

Wednesday, 16th

Royal Eye Hospital
5 30 P.M Mr H B Jacobs Relation of Nasal and Ocular Diseases.
Institute of Dermatology
5 30 P.M Dr J O Oliver Laboratory Diagnosis of Syphilis.
Institute of Urology 10, Henrietta Street, W C 2
5 P.M Dr A H Harkness Non gonococcal Urethritis.
Eugenics Society
5 30 P.M (Burlington House Piccadilly, W 1) Dr Hermann Lehmann *Distribution of Sickle-cell Trait in Africans* and Indian Aboriginals

Thursday, 17th

Royal College of Surgeons
3 45 P.M Dr J Stretton Young Benign Mammary Epithelial Hyperplasia. (Erasmus Wilson demonstration.)
Institute of Laryngology and Otology, 330, Gray's Inn Road, W C 1
5 P.M. Prof. F C Ormerod Anatomy of Paranasal Sinuses.
Harveian Society of London 11, Chandos Street, W 1
8 15 P.M Prof Alan Moncrieff Marasmus Dr R E Bonham Carter Congenital Heart Disease Dr B Schlesinger Infantile Diarrhœa

Friday, 18th

Royal Society of Medicine, 1, Wimpole Street, W 1
4 30 P.M *Section of Epidemiology* Dr P L McKinlay Cancer in Scotland
Royal Eye Hospital
5 30 P.M Prof. C A. Keele Local Anæsthetics in Ophthalmology
Institute of Dermatology
5 30 P.M Dr Bettley Clinical demonstration

Appointments

DOOLEY, C P, L R.C P I, D P H asst. school M O, Nottingham Education Committee
GLYNN J D L R C.P I, D P M asst psychiatrist Whittingham Hospital Preston
HARGREAVES BETTY M.B Lpool, M R.C O G consultant obstetrician and gynæcologist Wigan and Leigh Hospital Centre
ZWIEFACH, ELIASZ, M.D. Cracow, F R C.S D L.O consultant ear, nose, and throat surgeon West Middlesex Hospital Isleworth

South East Metropolitan Regional Hospital Board

DAVIES S W M.R C.S D.P M consultant psychiatrist and physician superintendent, Loybourne Grange group of hospitals.
EDRIDGE ANTHONY, M.R.C.S, D A consultant anæsthetist, Tunbridge Wells group of hospitals.
PERCHARD S D, M D Lond, M.R C.O G consultant obstetrician and gynæcologist, Orpington and Sevenoaks group of hospitals.
SOWDEN K A M D Lond D PHYS MED consultant in physical medicine Dartford Medway and Gravesend group of hospitals

Western Regional Hospital Board, Scotland:

CONNOLLY MARGARET L.R.C P.E, D A asst. anæsthetist, Glasgow Royal Infirmary
COWIE, T N M D Glasg, D M R.D consultant radiologist Western Infirmary, Glasgow
HILLIS B R M.D Glasg, M R C P F F R.F.P.S chest physician, senior asst to the area-supervising tuberculosis physician for the Dumfries and Galloway area and deputy physician superintendent of Lochmaben Sanatorium

GRAVITATIONAL ULCER

R B Wright
D.S O O.B E. B.Sc. Ch.M. Glasg,
F.R C.S E., F.R.F P.S

ASSISTANT SURGEON WESTERN INFIRMARY, GLASGOW

In all the field of medical practice there can be few conditions more perplexing to the physician and more troublesome to the patient than that recurring chronic ulceration of the lower third of the leg variously termed varicose ulcer non specific ulcer, or gravitational ulcer Such ulcers are characterised by the site of their occurrence—the gaiter area—and by the fact that they usually heal with rest in bed but tend to recur when the sufferer becomes ambulant There are great variations in size and severity of symptoms some of these ulcers are painful, some are not some are associated with obvious and gross varicose veins some are not; some are apparently related to previous deep venous thrombosis and some are not. The incidence of the condition is difficult to assess

The usual sequence of events in the development of gravitational ulcer is venous stasis → pigmentation of skin → induration → œdema → subcutaneous fibrosis → diminished local vascularity → minor trauma → indolent ulcer The induration which precedes the ulceration varies considerably in extent, from a patch on the anteromedial aspect of the leg to an encircling gaiter In the first type the patch of induration and later the ulcer often appears to sit astride a prominent superficial varicose vein—the feeder vein of Paré—this is the typical varicose ulcer of Brodie (1846) In the second type the ulcer may be single or multiple and at the same site, but there are often no evident associated varicose veins nor any history of such In some of these cases there is a clear history of antecedent deep vein thrombosis or superficial phlebitis and this type has been termed the postphlebitic ulcer by Homans (1916) and others

General Considerations

It is generally accepted that gravitational ulcer is due to venous stasis, but the ulcer rarely bleeds and is always set in a zone of increased subcutaneous fibrosis. The ulcer is usually in the lower third of the leg and on the anteromedial aspect, where Bellocq (1925) has shown that the arterial plexus of the skin has a very wide mesh and the vessels are of small calibre If the stasis is alleviated by rest or support in most cases the œdema resolves and the ulcer heals more or less soundly

Local stasis may be due to either arterial or venous insufficiency Arterial insufficiency alone may rarely lead to ulceration indistinguishable from gravitational ulceration.

The factors which influence the venous return from the lower limb are as follows

(1) Vis a tergo—the arterial inflow
(2) The pump action of the limb musculature which, to be most effective demands
(3) Soft compressible veins, and
(4) Competent vein valves.
(5) Heart action producing a suction effect in the cavity veins.

Gravity and obesity militate against these factors to various extents.

In the normal limb venous blood flow is always centripetal no matter what is the attitude or the activity of the patient, and this is ensured by valve competence Any factor which destroys or impairs valvular competence allows venous reflux and stasis.

Hæmodynamics

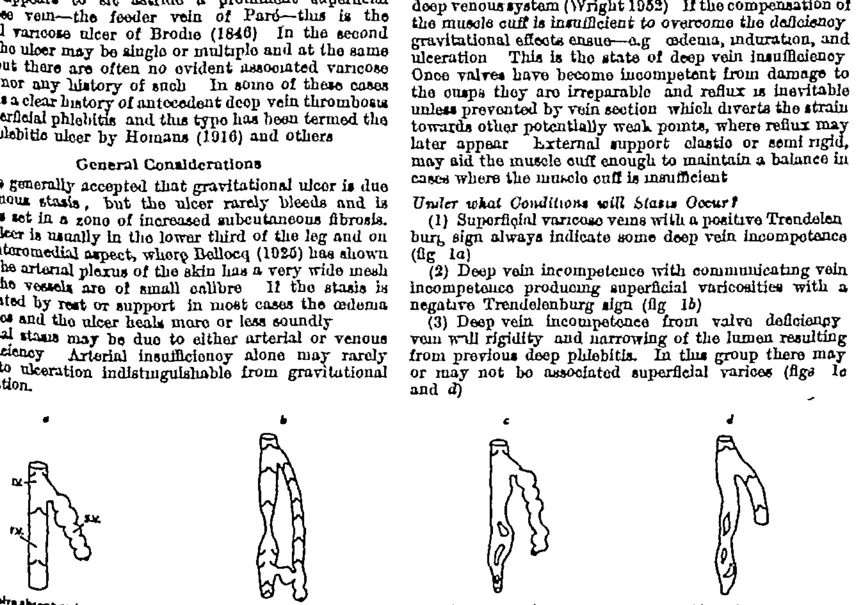
To obtain a normal deep venous return the deep vein valves must be competent, and the vein wall must be soft and elastic and surrounded by skeletal muscles capable of exercising a massaging pump action. Anything which interferes with valve action or pump action may produce stasis. Valve incompetence permits venous reflux, which will throw a strain on successively lower valves and ultimately on the valves of the communicating veins If these valves in turn become incompetent the strain will be transferred to the superficial system, and this is, I believe, the essential cause of most varicosities of the superficial veins—i.e. the primary defect is in the deep venous system (Wright 1952) If the compensation of *the muscle cuff is insufficient to overcome the deficiency* gravitational effects ensue—e.g œdema, induration, and ulceration This is the state of deep vein insufficiency Once valves have become incompetent from damage to the cusps they are irreparable and reflux is inevitable unless prevented by vein section which diverts the strain towards other potentially weak points, where reflux may later appear External support elastic or semi rigid, may aid the muscle cuff enough to maintain a balance in cases where the muscle cuff is insufficient

Under what Conditions will Stasis Occur?

(1) Superficial varicose veins with a positive Trendelenburg sign always indicate some deep vein incompetence (fig 1*a*)

(2) Deep vein incompetence with communicating vein incompetence producing superficial varicosities with a negative Trendelenburg sign (fig 1*b*)

(3) Deep vein incompetence from valve deficiency vein wall rigidity and narrowing of the lumen resulting from previous deep phlebitis. In this group there may or may not be associated superficial varices (figs 1*c* and *d*)



a:
valve absent or incompetent.
enous valve incompetent.
insufficiency localised.
ficial insufficiency extensive.
rficial varices.
Trendelenburg positive.
Ulcer uncommon.

b:
Normal iliac vein.
Normal upper deep vein.
Localised deep thrombosis with resultant
Localised deep insufficiency
Localised superficial varices.
Trendelenburg negative.
Ulcer uncommon.

c:
Iliac valve absent or incompetent.
Saphenous valve incompetent.
Deep-vein thrombosis with resultant
Extensive deep insufficiency
Extensive superficial varices.
Trendelenburg positive.
Ulcer common.

d:
Normal iliac vein.
Normal saphenous vein.
Deep femoral thrombosis with resultant
Extensive deep insufficiency
No superficial varices.
Trendelenburg negative.
Ulcer common.

Fig 1—State of venous valves in various conditions in which gravitational ulcer may develop: F V., femoral vein; I.V iliac vein; S.V., internal saphenous vein.

Gay (1868), in post-mortem dissection of ten legs the seat of gravitational ulcer, found the deep veins partially obstructed by thrombus in six cases and dilated and tortuous in three He also noted that "after deep thrombosis the channels are to a great extent restored by contraction of the clot and eventually organic combination with the vein wall"—a simple fact often lost sight of to this day

It seems clear that the deep veins are the most important element in the venous system of the leg, and that in gravitational ulcer one must treat the deep-vein insufficiency while accepting that some degree of underlying deep-vein valve incompetence is permanent

Demonstration of Reflux

Demonstration of reflux into the superficial veins is usually easy The Trendelenburg (1881) test is positive in most cases of varicose veins when first seen (Wright 1950) Further, in almost all such cases a cough impulse can be felt in the saphenous vein, indicating that increases of intra abdominal pressure are being transmitted to the superficial veins of the limb and, therefore, that at least the iliac valve and first saphenous valve must be incompetent

The regularity with which varicosities of the internal saphenous vein will recur, from above, after high ligation operations, unless the internal saphenous vein is tied flush with the femoral vein above all tributaries, is striking (Wright 1949) Abdominal reflux into the internal saphenous vein can only be prevented by ligation at the sapheno-femoral junction If superficial varices recur after adequate high ligation, reflux through incompetent communicating veins will be demonstrable and can be prevented by division of such communicating veins This, again, confirms that the primary fault is in the deep veins When superficial varices recur after treatment they are recanalised from above downwards, and this is so after inadequate ligation and after sclerosing injection and also after spontaneous thrombosis. All these facts emphasise that the primary defect is in the deep veins and that superficial varices are a reflection of deep-vein incompetence

Prevention of Reflux

Reflux into the main superficial veins can be prevented by division of the veins surgically at their points of entry into the deep veins (Homans 1916)—to be effective this must be done exactly at these points (Wright 1949)—and by section of incompetent communicating veins Stasis in the superficial plexus can thereafter be reduced by obliterating these veins by either sclerosant injection or excision

Sclerosant Injection

Sclerosing fluid injected with the intention of producing a chemical phlebitis carries the danger of damage to the deep veins and communicating veins and their valves Experience shows this to be a theoretical risk, provided the sclerosant is viscid and is injected high and in small volume, and the patient's muscle tone is not reduced by general anæsthesia

Radiography after experimental injection of a radio-opaque sclerosing fluid similar to that used by Boyd (1948) showed that the fluid passed very rapidly into the deep veins through competent communicating veins in the upper thigh In the deep veins this spill is rapidly diluted and dispersed, and damage to valves is likely to be minimal If the fluid is injected at a high level, escape through high communicating veins will only tend to damage the upper femoral or iliac valves, which in almost all cases are already demonstrably incompetent This, of course, does not happen if the fluid is injected below the knee, as advised by Boyd and Robertson (1947), when many deep vein valves may trap the sclerosant and be damaged

Location of Communicating Veins

Numerous tests, all theoretically sound, have been described for the location of incompetent communicating veins All regard the venous system of the lower limb as if it were a large U tube with a varying number of inter communications between the two limbs—the saphenous vein and the femoral vein—running more or less horizontally But this is not so The course of communicating veins may be long and tortuous They are of two types (Warwick 1931) (1) direct, commonly relatively short, and often paired (fig 2), which connect the main saphenous trunks with the main deep veins, and (2) indirect, usually tortuous, and oblique, which unite tributaries of the saphenous veins with the deep veins via their intramuscular tributaries (fig 2) Though there are certain sites at which direct (Boyd and Robertson 1947, Wright 1950) and indirect (Gay 1868, Cockett and Jones 1953) communicating veins are commonly found, there is no constant number or location of either type

Œdema, the coarse subcutaneous fat above the knee, induration below the knee, the high tension in the incompetent saphenous vein on straining, and the presence of two bones in the deep compartment of the leg often make adequate compression of the superficial veins with a tourniquet difficult or impossible without seriously impeding the flow in the deep vessels The tourniquet tests of Ochsner and Mahorner (1936), Perthes (1895), and Slavin (1948) have all been tried but found lacking for the reasons detailed In more than one patient with gross superficial varices a pneumatic tourniquet was placed about mid-thigh and pumped up to a pressure of 140 mm Hg and then a small volume of 25% 'Pyelosil' was injected into the saphenous vein above the tourniquet, which was slowly deflated while the limb was watched on the X-ray screen In many cases, at a pressure of 100–120 mm Hg, the pyelosil was seen falling down inside the tourniquet—the patient was standing erect but not straining This provides a clear demonstration of the fallacy of believing the tourniquet to be "tight enough to occlude only the superficial veins without impeding the flow in the deep vessels."

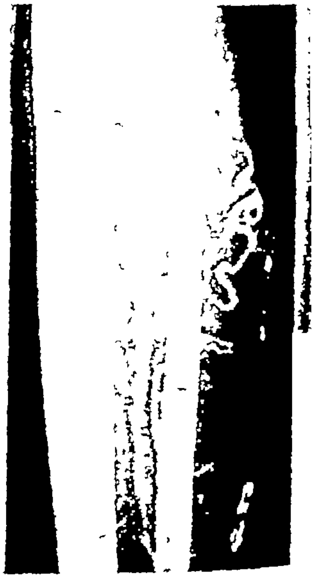


Fig. 2—Ascending venogram showing paired direct and tortuous indirect communicating veins.

The most accurate method of locating communicating veins is venography, but this is expensive and time-consuming and to be of value requires a special and not easily acquired technique (Dow 1951) Though it is possible to demarcate accurately by venography the anatomical distribution of communicating veins, it is by no means easy to demonstrate convincingly which are incompetent

In cooperation with Dr J D Dow comparisons between clinical, venographic, and operative findings were made in a large series of cases of varicose veins, and the following *practical clinical method* of locating communicating-vein incompetence was developed

The Trendelenburg test is first applied to demonstrate the presence or absence of abdominal reflux The test is then repeated, and the pressure at the fossa ovalis maintained for a full minute while the superficial veins are observed If there re no grossly incompetent communicating veins, the super icial veins fill slowly and uniformly from below If superficial rarices appear immediately or rapidly the leg segment is noted and also whether there is obvious reflux from above ese level

The patient is then instructed to exercise the calf muscles actively If the varices become more full and tense the communicating vein valves are incompetent. If the superficial varices fill from above the knee the level of digital compression is lowered to the level of the adductor tubercle and its adequacy is tested by applying the cough impulse test with a watching finger on the line of the main trunk distally and the test is repeated The actual site of emergence of the communicating vein through the deep fascia can often be felt with a finger tip especially in the case of indirect communicating veins.

If such a fascial defect is felt, the test is repeated with one finger occluding the main trunk at the fossa ovalis and another the defect in the deep fascia If this lower finger is at the site of emergence of the incompetent communicating vein the varices will not appear until the finger is removed. In cases where the Trendelenburg test is negative this latter test is still applicable.

Cockett and Jones (1953) have drawn attention to the importance of incompetent indirect communicating veins in the lower third of the leg and noted their relationship to the site incidence of certain gravitational ulcers, as was noted by Gay (1868) in his post-mortem dissections. But not all ulcers occur at these sites, and not all patients who have such communicating veins develop ulcers. Demonstrably incompetent communicating veins should be sectioned deep to the deep fascia, and the defect in that layer sutured (Wright 1950) Wounds in the indurated gaiter zone can be very troublesome, and healing a lengthy process. Dissection in the subcutaneous tissue should be avoided as far as possible, and the communicating veins secured beneath the deep fascia, where dissection is much more easy (Wright 1950) Excision and primary suture suggested by Cockett and Jones (1953) is likely to lead to many troublesome wounds and can rarely be advisable or applicable

Subcutaneous stripping (Mayo 1906) of the main internal saphenous trunk will sever direct communicating veins, but the more important and troublesome indirect communicating veins will rarely be affected. This appears to be a definite defect of this popular method of eliminating superficial varicosities. Further it leaves the defects in the deep fascia through which further blow outs can develop

Deep Veins

Whereas the superficial veins can be easily and directly studied the assessment of the state of the deep veins is difficult and their rôle in the ætiology of gravitational ulcer has occasioned considerable comment (Homans 1916 Bauer 1940 Anning 1950) Many regard permanent deep-vein blockage to be the usual late result of deep thrombosis, and associated varicosities of the superficial veins as an overdistended but necessary collateral circulation (Franklin 1937, Ochsner and Mahorner 1939 Rogers 1939 Coombs 1940 Foote 1944 Anning 1950, Rivlin 1951) But not all cases of previous deep vein thrombosis develop varices, and seldom is there evidence of multiple blow outs of communicating veins, which would be necessary to permit reflux into the superficial veins at all levels of supposed blockage Further the direction of blood flow in superficial varices is retrograde when the upright posture is assumed, and usually freely so on coughing or straining

The incidence of varices and the time-incidence of thrombosis or phlebitis in 284 consecutive cases of gravitational ulcer seen at the varicose vein clinic in the Western Infirmary Glasgow is shown in table I. In only 37 cases was there definite or presumptive evidence of preceding deep thrombosis, and in 27 of these the patients had noted superficial varices before the incident of deep thrombosis. In 48 there was a history of antecedent superficial phlebitis but in only 3 of these cases did the patient claim that the varices followed the phlebitis In a separate series of 35 cases of puerperal white leg in 1925–45 only 16 of the patients had any sign of superficial varicose veins and, of these, 6 stated categorically that their varices had been present for several years before the incident of puerperal thrombosis. The remaining 10 stated that their varices followed the thrombosis.

TABLE I—RELATIONSHIP OF PHLEBITIS TO VARICOSE ULCERS

Sex	No of cases	With varices	With history of deep thrombosis	History of deep thrombosis plus previous varices	With varices which followed thrombosis	With previous superficial phlebitis	With varices which followed superficial phlebitis
M	98	95	10	5	2	17	2
F	186	181	27	22	5	31	1
Total	284	270	37	27	7	48	3

I have observed 2 cases in which the femoral vein had been divided and injected in retrograde manner with a sclerosant. In neither case did new varices appear, and the resulting œdema in 1 has been improved by extirpation of previously present superficial varices. The other patient a young adult male has gradually developed an adequate collateral circulation and the œdema has disappeared

After superficial phlebitis occurring naturally or chemically induced, as in the injection treatment of varicose veins, recanalisation of the thrombus is the rule and, in cases of varicose veins can be observed to progress from above downwards. Such thrombus is much more adherent to the vein wall and associated with more severe toxic or chemical damage to the intima than is the 'quiet' thrombus of deep thrombosis, and would be expected to produce more permanent obliteration of the lumen Experience shows that to obliterate permanently the lumen of a vein subject to stress without destroying the entire vein wall is virtually impossible

For these various reasons recanalisation of deep veins is to be expected after deep thrombosis. Though a complete persistent block is not to be expected a reduction in deep vein efficiency is certain and it seems helpful in attempting to formulate rational treatment, to try to assess the degree of this deep-vein insufficiency

Perthes's Test

The popular test used for this purpose—and it is usually regarded as a test for deep vein blockage (Rivlin 1951)—is Perthes's test

> A venous tourniquet is applied below the level of the lowest incompetent perforating vein so as to occlude the superficial but not the deep veins. The patient then walks briskly about for three or four minutes. If the deep veins are thrombosed then the occlusion of the superficial veins by the venous tourniquet has shut off the only route by which the limb blood can return to the heart and as the patient walks, the veins below the tourniquet do not decrease in size and may even swell and cause pain

This test is quite impractical for many reasons the lowest incompetent perforating vein may be at or below ankle level, the induration of the lower leg may make compression of the superficial veins with a tourniquet impossible without so impeding both arterial inflow and deep venous return as to cause pain and distension of varices without exercise and venous reflux in incompetent varicose veins on exercise can cause distension below an inefficient tourniquet. A modification of this test was used in the location of incompetent communicating veins, themselves an indication of deep incompetence, but it could not be used to assess the degree of deep vein insufficiency of other nature.

In a postphlebitic limb with varices, if the main varicose trunk is occluded at the saphenofemoral junction and the limb is elevated, the veins empty rapidly Similarly, if a varicose segment is isolated between two superficial tourniquets (Warwick 1931) and the limb is elevated, the loop rapidly empties Both these tests demonstrate that a deep venous circulation is patent, this may be either a recanalisation of the previously thrombosed veins or a collateral circulation At operations for varicose veins in postphlebitic cases, if opportunity is taken to explore the femoral vein, in many cases it appears normal, in others it is thickened and matted to the femoral sheath, but even in such cases blood-flow in the vein can always be demonstrated by digital stripping, showing that at least partial recanalisation of the main vein is usual

Venography

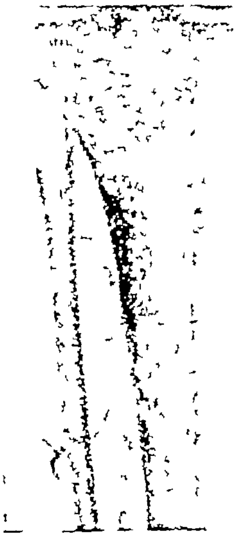


Fig 3—Ascending venogram in patient who had deep-vein thrombosis 17 years previously and gravitational ulcer for 10 years showing patent deep trunk indistinguishable from normal

Two further methods of investigating the deep veins have been advocated venography and pressure tests By ascending venography, provided a proper technique is used to compress the superficial-veins, a patent main deep trunk is invariably demonstrable (fig 3), it is impossible to decide definitely on the efficiency of this deep trunk The technique, difficulties, and interpretation of ascending and descending venography of the deep veins have been very thoroughly discussed by Dow (1951) There appears to be no constant relationship between venographic appearances and the clinical severity of post-thrombotic sequelæ The technique is difficult and time consuming, and is valuable only as a means of confirming impressions of pathology It adds nothing to the problem of treatment, nor is it profitable as a routine investigation

Pressure Tests

The pressure in the veins of a normal lower limb at rest corresponds to a column of blood from the level concerned to heart level (Smirk 1936, Pollack and Wood 1949, Walker and Longland 1950) Thus, the pressure in a vein of the foot in a man of average height standing at rest is about 90 mm Hg During exercise the muscle-cuff pump lifts the blood from the foot towards the heart, and in normal people the pressure in a foot vein falls to about 20–30 mm Hg In varicose veins, on exercise, varying abdominal pressure forces blood down the saphenous vein by reflux, and the pressure fall on exercise may be small or nil, or there may be a fluctuating rise If a tourniquet is applied below the knee (Walker and Longland 1950) to prevent such reflux, the exercise fall is near normal, but very variable results are obtained because of the usual venous tourniquet difficulties

Theoretically, in deep vein insufficiency, if the superficial reflux could be eliminated without affecting the deep return, the height of the pressure reading on exercise above normal would be a guide to the degree of stasis in the deep circulation—i e of deep insufficiency Unfortunately in the cases where this test might be of most value the presence of high tension varices and, especially, the gross induration of the lower limb and reflux through incompetent communicating veins below the knee render the test invalid The procedure, involving intubati of a superficial vein on the dorsum of the foot with 'Polythene' tube filled with citrate solution and co nected to a manometer, is clearly not a simple bedsi or outpatient procedure Being subject to so ma fallacies it was abandoned after a brief trial because did not provide any information not already known

It becomes clear that there is no test of deep-ve insufficiency of real practical value But cases of gra tational ulcer can be classified in three groups of ascendi difficulty in management

(1) Cases with superficial varicose veins and no history deep thrombosis

(2) Cases with superficial varicose veins and a history deep thrombosis

(3) Cases with no varices and a history of deep thrombos

Alternatively another classification might be follows

(1) Deep vein incompetence with no impediment to de return other than venous reflux

(2) Deep vein incompetence with impediment to de return in addition to reflux.

Scheme of Treatment

On the basis of the foregoing conclusions the followi standard method of management of gravitational ulc was adopted in 284 consecutive cases

(1) The ulcer was encouraged to heal by applying a pr tective non adhesive dressing of tulle gras Over this w applied a pad of orthopædic felt to exert local pressure, t disperse œdema, and so to help restore the local vascularit and the limb was firmly encased in a semi rigid boot 'Viscopaste' from the base of the toes to just below the kne Such dressings were applied weekly until œdema was disperse and then less frequently until the ulcer healed or became stati No antiseptics were used, nor did they seem necessar Viscopaste was preferred to 'Elastoplast' because it is eas to apply and less likely to cause distressing skin reactions. a skin reaction did develop, the limb was swathed in gau soaked in 5% 'Ichthyol' in calamine lotion, and the visc paste was applied on top The patient was kept ambulant encourage deep venous return.

(2) Superficial varicose veins were treated by appropria ligation and retrograde injection of sclerosant solution. almost all the cases this was an outpatient procedure do under local anæsthesia

(3) Demonstrably incompetent communicating veins wer divided beneath the deep fascia, which was then sutured.

(4) Deep venous return was encouraged by the provisio of semi rigid viscopaste support and by keeping the patien ambulant, by encouraging reduction of obesity, and b providing elastic stockings to be worn after healing had bee achieved

As will be recounted later, further measures were onl applied if the standard treatment failed or was foun inapplicable

Table II shows the treatment applied in this series, an table III a comparison of results with other publishe series It must be emphasised that the present series from a varicose-vein clinic and contains a very hig proportion of cases with superficial varices, in othe series the incidence of varices may be much lower, and o previous thrombosis much higher This will influence th success-rate very considerably

TABLE II—METHODS OF TREATMENT

Treatment	No of patients		
	Men	Women	Total
High ligation and retrograde injection	35	62	97
High ligation retrograde injection and communicating vein ligation	49	102	151
Communicating vein ligation alone	4	4	8
Support alone	9	14	23
Skin grafting	—	4	4
Deep vein ligation	1	4	5

Though dispersal of œdema and support of the muscle cuff formed the initial basis of treatment two additional observations emphasise the value of elimination of coexisting superficial varices

It is well known that gravitational ulcers naturally tend to heal with rest in bed or support of the limb, and to recur if these measures are withdrawn To try to assess the contribution of superficial vein ligation, a series of cases was treated by "immediate ligation and no local support Of 12 cases so treated all were successful, the average healing time being six weeks In none of these cases was there any history of phlebitis

Further corroboration of the value of eliminating the effects of reflux was provided by 6 cases with gravitational ulcer superficial varices, and a negative Trendelenburg test (table IV) In none of these was there a history of antecedent thrombosis or phlebitis, and in all of them sound healing of the ulcer followed ligation and division of incompetent communicating veins The site of the blow-out varied in 4 cases it was on the calf and in the remaining 2 it corresponded to the posteromedial indirect communicating vein described by Cockett and Jones (1953) Warwick (1931) and Gay (1868) These cases confirm the value of the elimination of local reflux into the superficial veins.

Examination of the 14 cases in which ulceration recurred after healing revealed blow outs in 11 of them. In all of these appropriate ligation led to healing Of the remaining 3 patients 2 have been subjected to femoral vein ligation combined with skin grafting with ultimate success in 1 the other patient underwent popliteal vein ligation and skin grafting, with great success.

TABLE III—COMPARATIVE RESULTS

Reference	No. of patients	Remaining healed (%)	Length of follow up (mos.)
Buxton and Coller (1945)	26	87·0	3–6
Linton and Hardy (1948)	84	81·0	1–16
Glasser (1949)	40	72 5	6–48
Bauer (1950)	196	84 0	0–36
Present series	284	93 5	12–60

In 16% there was a recurrence, and almost two thirds of these "seemed to be due to persistent incompetent veins in the superficial system" (Bauer's comment on his series treated by popliteal-vein ligation).

Discussion

The effects of thrombophlebitis in any part of the venous system are damage to the intima, valves, and vein walls, with in the acute phase, complete blockage of the lumen by thrombus. Later as resolution takes place, fibrosis of the valves walls and thrombus produces valve incompetence, loss of elasticity and recanalisation The end result is vein incompetence with narrowing of the lumen—a state of venous insufficiency, compensation for which must be obtained by adequate collateral circulation if a normal venous return is to be achieved. Whether this last can be achieved or not depends largely on the extent of the thrombophlebitis and the previous competence of the affected veins

Deep vein thrombosis may develop in patients with previously normal veins or with superficial varices From clinical observation it seems that the presence of superficial varicose veins, itself an indication of deep vein incompetence (Wright 1952) may well indicate a predisposition to the development of deep vein thrombosis In this series of 284 cases of gravitational ulcer there was a history of definite or probable deep vein thrombosis in 31 and 27 of these had a clear history of previous varicose veins. In only 7 did the history indicate that the varices had followed the thrombotic incident.

The damage to the deep veins inflicted by thrombosis is essentially threefold (1) loss of valves, allowing venous reflux ; (2) loss of calibre, causing impediment to blood flow, which will affect both onward flow and reflux ; and (3) loss of elasticity, diminishing the efficiency of the massaging effect of the muscle cuff pump

TABLE IV—CASES TREATED BY LIGATION OF COMMUNICATING VEINS

Case no	Duration of ulcer	Site of blow-out	Period healed (yr)
1	10 yr	Calf	4
2	6 wk.	Calf	5
3	4 mos.	Calf	2–5
4	3 yr.	Ankle	3
5	2½ yr	Calf	5
6	2 wk	Ankle	4

Bauer (1940) believes that the superficial venous system represents the usual collateral return in blockage of deep veins by thrombosis His claim (Bauer 1946) that recanalisation hardly ever takes place after deep thrombosis and that 'for the rest of life drainage is from deep to internal saphenous vein and upwards is based on his venographic studies and is contrary to necropsy (Gay 1868) and clinical findings (Warwick 1931) Dow (1951) never failed to show a patent deep circulation in post thrombotic legs, provided he compressed the superficial veins enough to force the radio opaque fluid into the deep veins. Bauer (1950) also claimed to be able to demonstrate deep vein incompetence by retrograde venography, and other workers have made similar claims. Dow has clearly shown that the appearances described by Bauer as indicating deep vein valve incompetence may be obtained in normal limbs when Bauer's technique is used It seems unreasonable to assume that a sudden tilting of the patient to 45° should cause the blood flow in the femoral vein to cease. Indeed if the femoral vein is opened at operation and the proximal end occluded profuse hæmorrhage leaves the witness in no doubt of the continuing upward flow of blood from the limb Further, the retrograde venogram is not a picture of a flowing stream but of a dense radio-opaque fluid percolating downwards through an upward flowing stream of blood.

Deep vein ligation and split skin grafting were only used in this series if elimination of superficial vein reflux and stasis plus elastic support failed to achieve sound healing and to compensate for the continuing deep vein defects. Interruption of the deep veins has had many advocates (de Takats et al 1929 Leriche 1926 Buxton and Coller 1945 Linton and Hardy 1948 Bauer 1948 Glasser 1949) Though there is no doubt that recanalisation is the rule after deep thrombosis the resulting lumen is narrowed tortuous, and valveless and the vein wall is thickened rigid, and matted to the artery and often to the accompanying nerves, all of which share in the inflammation. Thus, nerve irritation artery irritation lymphatic involvement, and sympathetic-*nerve involvement may all play a part in the production* of signs and symptoms It is consequently difficult to assess the results of the various procedures advocated for the relief of deep vein insufficiency Single interruption at any level will only prevent reflux at that level, and reflux via collaterals may still take place.

In my limited experience the most constant effect of deep vein ligation has been relief of bursting pain this suggests a nerve section effect presumably sympathetic Postoperative flushing of the foot and ankle in these cases also suggests a sympathetic nerve-section effect Œdema has never completely subsided

If reflux were the only deep vein defect deep vein ligation would seem to be a sound procedure although it would usually require to be done at several levels to defeat the effect of by passing Deep venous reflux as a primary defect may lead to the development of superficial varicose veins but many cases with extensive superficial varices never develop ulceration, and those that do always show evidence of some preceding thrombosis of at least a perforating vein Deep thrombosis may be followed by gravitational ulceration in limbs where there are no superficial varices Thus it seems that the determining factor in the production of ulceration is something more than incompetence of deep or superficial veins—i e , deep-vein insufficiency the result of thrombosis When there is superficial vein as well as deep-vein insufficiency, the removal of the effects of the former proves beneficial to the limb and may so relieve stasis as to permit sound healing of gravitational ulceration and reduction in œdema and induration Varicose veins are not a cause of ulceration All gravitational ulcers are postphlebitic, although there may be no history of characteristic deep-vein thrombosis and the extent of the deep phlebitis may be quite localised

The nature and degree of deep-vein insufficiency cannot be accurately assessed or located clinically or by ancillary methods Reflux in superficial and communicating veins can be prevented by vein section, but to apply this procedure to deep veins produces a block not only to deep vein reflux but also to the deep venous return The collateral circulation established to circumvent such a block may in turn be submitted to the strain of femoral or iliac valve incompetence and itself become incompetent Fibrosis and loss of calibre, the result of thrombosis, will stimulate the opening up of a collateral circulation, and it seems that this can best be aided by supporting the muscle cuff and eliminating the effects of gravity Rest in bed is economically impossible for many of these patients and in any case tends to encourage stagnation Ambulatory treatment seems the most reasonable prophylactic against deep-vein stagnation, just as continued elastic support seems to be the fundamental requirement of treatment

Summary

The factors responsible for venous stasis in the lower limb are discussed, and the particular importance of valve competence and the massaging effect of the muscle cuff of the leg are emphasised

Superficial varicose veins are a consequence of deep vein insufficiency, which in certain cases also causes œdema, induration, and ulceration

Methods of demonstrating and locating the sites of reflux into the superficial veins are described Such reflux can be prevented by appropriate vein section

The value of sclerosant injection in the elimination of stasis in the superficial veins is considered Damage to the deep veins is unlikely if the sclerosant is viscid and is injected high and in small volume

The effects of thrombosis on the deep veins are diminution of lumen, increased rigidity, and loss of valves Recanalisation is the rule The value of venography and pressure tests in attempting to assess the state of the deep veins is critically discussed Neither procedure helps in the problem of treatment

284 cases of gravitational ulcer were treated by elimination of superficial varices and with semi rigid supporting bandages 93 5% remained healed for 12–66 months

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VAGINAL BLEEDING DUE TO POTASSIUM PERMANGANATE

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THE relative scarcity of published reports of traumatic vaginal hæmorrhage due to ulceration by potassium permanganate gives a wrong impression of the true incidence of a not uncommon condition Doctors who see cases do not often report them , but, since the bleeding can be so copious as to threaten life, it has been thought advisable to publish this new series of cases.

Potassium permanganate is a common disinfectant, and common disinfectants tend to be introduced into the vagina This does not matter much, so long as they are adequately diluted, but in strong concentrations any antiseptic can cause disaster to the woman using it.

It is believed that potassium permanganate in contact with the moist vaginal wall is broken down to potassium hydroxide (caustic potash) and to manganese oxide or oxides The potassium hydroxide causes deep ulceration, and the manganese oxides can have severe toxic effects The ulcers bleed, giving rise to deceptive and sometimes dangerous hæmorrhage

In 1951–53 eleven patients who had had vaginal bleeding following the misapplication of potassium permanganate were admitted to Oldchurch Hospital. One would have lost her life if a blood transfusion had not been given on admission and if the correct diagnosis of the condition had not been made This minor epidemic resulted from a local belief that potassium permanganate tablets or crystals could bring about abortion

The tablets and the crystals were bought by the patients at two local chemists, but one patient received the tablets from her mother as a gift on her wedding eve The permanganate produced severe burning where it settled in the solid state , in the vagina clean but very indolent ulcers resulted and small arteries were eroded, with resultant bleeding that was sometimes difficult to arrest Secondary hæmorrhage was a feature of the severer burns, and healing was accompanied by thick scarring

As an abortifacient potassium permanganate is virtually useless, for abortion rarely results unless a permanganate

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solution is introduced into the uterus There are only two reported cases of intra-uterine douching with saturated potassium permanganate solution These were reported by Jetter and Hunter (1949), and in both of them the douching proved fatal to the mother The permanganate was shown to be not only an ulcerating agent and a burning agent but also a hæmolytic agent

In reports from other sources it has been suggested that heavy bleeding from the vagina in association with an enlarged pregnant uterus misleads the unwary gynæcologist into diagnosing inevitable abortion and perhaps even performing uterine curettage.

At Oldchurch Hospital conservative treatment of abortion is practised, and those women who bleed and whose bleeding is not soon controlled are carefully examined in the ward to exclude trauma of any sort before surgery is contemplated Even in inevitable abortion conservative measures are usually taken Thus, all the cases of potassium permanganate burns in the present series were diagnosed by discovery of the ulcers in spite of the almost invariable absence of a history of trauma. When confronted with the diagnosis all the patients confirmed it.

The treatment consists in removing the tablets or crystals washing away the manganese oxides that have formed and taking any steps necessary to control the hæmorrhage. Surgery may be necessary to undersew the ulcers with deep mattress stitches—which can be difficult, because the ulcers are often situated in the highest part of one of the lateral fornices.

Illustrative Case records

Case 1.—A married woman, aged 28 was admitted on Dec. 25, 1951 When her period was a week overdue the patient used a ' potash ' tablet and next day had a fairly severe primary hæmorrhage. A week later further bleeding started. When she was admitted to hospital a deep ulcer on the posterior wall of the vagina and another on the anterior lip of the cervix were found The patient's pulse-rate was 116 It was estimated that she had lost more than 2 pints of blood, and, as the bleeding was continuing briskly the ulcers were sutured in the operating theatre under general anæsthesia. A pint of 'Plasmosan' and a pint of blood were transfused. Two days later the hæmoglobin was 54%. The patient was discharged on Jan. 6, 1952.

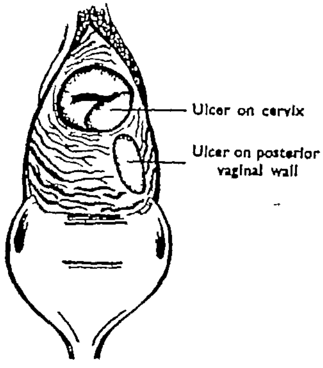
Case 2.—A married woman, aged 29 was admitted on April 3 1952. When her period was four weeks overdue she took twelve Dr Armstrong's pills ' A few hours later she inserted some potassium permanganate crystals on cotton wool into her vulva. Within a few minutes she felt a very acute burning sensation in her vulva and vagina, and later in her abdomen and back. When she was admitted to hospital, her labia were œdematous. There was so much pain that it was impossible to pass a speculum Under general anæsthesia the crystals which had been converted into black manganese oxides, were removed and the vagina was washed out with a ½% solution of cetrimide. Flavine emulsion dressings were applied to the labia and lower vagina. These dressings were changed daily For the first few days every change of dressing caused slight bleeding. The patient was three weeks pregnant on admission and eight weeks pregnant on discharge on May 12.

Case 3.—A married woman, aged 32, was admitted on May 27 1952. When eight weeks pregnant she inserted a potassium permanganate tablet high into her vagina. This caused such profuse bleeding that two days later her doctor thought he saw the fœtus passed. When the diagnosis had been made after admission to hospital, the vagina was packed. When the pack was removed, the reactionary hæmorrhage was so severe from the right side of the cervix and the right vaginal wall that the ulcers had to be undersewn under general anæsthesia. The patient remained pregnant. She was discharged on June 8.

Case 4.—A married woman, aged 37, was admitted on July 18, 1952 She had inserted permanganate crystals into her vagina during the eighth week of her pregnancy A burning sensation and severe pain resulted. Her temperature was 103.4 F hæmoglobin 66% Treatment consisted in douching with warm water until all the crystals were dissolved away Chloramphenicol therapy was given. The patient was discharged on July 30 She remained pregnant and was delivered on March 1 1953 of a normal full size male infant The delivery was normal in spite of some scarring of the lower part of the vagina.

Case 5—A married woman aged 28, was admitted on July 31 1952 When her period was two days overdue she inserted a tablet of potassium permanganate into her vagina, and she was admitted a few hours later There was only slight vaginal loss, and this soon ceased The registrar who examined her had never seen the condition before He noted that she had a slight ulcer on her cervix but doubted whether she was pregnant. He discharged her from hospital six days after admission.

Two days later on Aug 7 the patient was readmitted virtually moribund Her blood pressure was 60/40 mm Hg Her pulse-rate was uncountable, and she was suffering from air hunger An immediate transfusion with two pints of plasmosan and a pint of blood was given before the patient was fit enough to be taken to the operating theatre There two ulcers were found, one on the cervix and one in the vagina; these were undersewn (see figure) and the vagina was packed. Next day the patient's temperature was 104°F On Aug 13 a loss recurred and persisted till Aug 15 when a further blood transfusion was necessary and the patient was returned to the operating theatre where under general anæsthesia the ulcers were re-sutured, this time with Nylon sutures. A urinary infection developed and was treated.



Ulcers in case 5 seen on examination with vaginal speculum.

The patient was discharged from hospital on Aug 30 after removal of the nylon stitches. She had not been pregnant at all. The absence of pregnancy was confirmed at the second operation, when blood was seen to be issuing from the cervix and normal menstrual curettings were obtained.

Case 6.—A married woman, aged 32, was admitted on July 29 1953 When her period was two weeks overdue she inserted a potassium permanganate tablet into her vagina. Her doctor diagnosed cervicitis he prescribed ethisterone to stop the bleeding and this treatment appeared to have been fairly successful in that the hæmorrhage which had been heavy on July 15 virtually ceased fourteen days later

When the patient was seen at the gynæcological clinic, a typical potassium permanganate ulcer was found in the right fornix. From fear of secondary hæmorrhage the patient was admitted to the ward Hæmoglobin was then 94%. No treatment was given.

On Aug 6 she was examined with a speculum to ascertain whether it was safe to discharge her This manœuvre caused a sudden blood loss of three pints. The bleeding ceased on the administration of morphine just before arrangements were completed to take the patient to the operating theatre. Four days later the hæmoglobin was 53%. Intravenous iron therapy was given. Further examination with a speculum on Aug 19 showed scarring in the right fornix There was no further bleeding

On Sept. 3 the patient was seen in the follow up clinic. She was still pregnant, her uterus being enlarged to the size of an eight-week pregnancy

Discussion

This condition is by no means new Its introduction into this country is blamed on the Americans, probably unfairly, but the first cases reported in England seem to have been in the vicinity of American aerodromes Not many reports have been published on this subject, but I have found fourteen in French and Italian written in the last ten years, and six in English On the Continent the condition seems to be fairly well recognised. The largest series reported, however, comes from America, where McDonough (1945) saw sixty-five cases, of which six ended in abortion Of ten cases seen by Lubin and Waltman (1951) between 1946 and 1949 only one ended in abortion Miller (1951) reported some ten cases from the Croydon area, and Henderson and Watt (1951) said they had seen several cases, three of which had required cæsarean section because of late scarring of the vagina The ulcers always heal with scarring

In an attempt to stop the misuse of potassium permanganate which started in the Romford district five or six years ago, my predecessor informed the police in 1951, and only one case occurred in that year I informed the police towards the end of 1952, and they tried to discourage the sale of potassium permanganate (by methods best known to themselves) There are no legal grounds for prohibiting the sale, so a new case was seen, after an interval of ten months, in 1953

The main danger of the condition lies in the fact that the diagnosis can be so difficult, because even fairly careful examination with a speculum by a doctor unfamiliar with the condition may fail to reveal an ulcer in the fornix of a lax vagina A further danger is the indolence of the ulcers and the fact that if they are even slightly disturbed, as by passing a speculum (as in case 6) or by intercourse, they may bleed profusely and the patient may be in danger of losing her life

In the present series no patient died, but one was quite lucky to escape with her life and had to have two operations All the patients were married Two aborted, neither as a result of using potassium permanganate I have seen stenosis of the vault in a patient who was treated at Oldchurch Hospital for potassium permanganate burns in 1949, and it is quite possible that stenosis will develop in some of the cases reported here

The accompanying illustration was drawn by one of our London Hospital medical students, Mr H M. Thomas, and it is taken from the operation findings at the first operation on case 5 I wish to thank Mr John D Watt, my senior colleague, who told me about the condition and made the diagnosis for me in the first case I saw, Sister J Holmes, of B2 Ward, Oldchurch Hospital, for her care in nursing all these patients, and Mr G H Bancroft-Livingston, who helped me in the preparation of this paper

Addendum

Since preparing this paper I have seen three further cases admitted to hospital, and a fourth case not requiring admission This brings the number of cases in this series to fifteen

One of the patients admitted was the first in this series to attain her aim she persuaded the registrar to curette her as a case of inevitable abortion It was only on removing the Auvard speculum and completing the curettage that he found the vaginal ulcer situated 1 in from the vulva and bleeding heavily This ulcer had caused a large blood clot to form, filling the vagina and the external cervical os In this case a therapeutic abortion would possibly have been justified, for the patient was an ill woman with two young children, who at the onset of her pregnancy already had such complex rhesus agglutinins that her blood had to be cross matched with that of seven donors to find the pint of fresh blood that eventually saved her life

In a valuable recent paper Alment and Nicol (1953) reported five cases, and rightly pointed out that the permanganate lesions could be confused with primary chancres

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TREATMENT OF MEGALOBLASTIC ANÆMIAS

RELATION OF PENICILLIN TO VITAMIN B_{12}

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We have previously reported the responses of the megaloblastic anæmias in Africans to oral or intramuscular penicillin (Foy et al 1951, 1952a, b, and c), and shown that these responses in every way resemble those obtained in similar types of anæmia by the use of potent hæmatinics

It is well known that whereas all megaloblastic anæmias respond to folic acid, not all respond to vitamin B_{12} In this paper we show that those anæmias which do not respond to penicillin do not respond to vitamin B_{12} by mouth, and we suggest that penicillin acts in the megaloblastic anæmias by stimulating the biosynthesis of vitamin B_{12} by the intestinal microflora

All the cases selected for treatment were severe megaloblastic anæmias with red cell counts of 500,000–2,500,000 per c mm, megaloblastic bone marrow, giant stab-cells, and the mean corpuscular volume (M C.V) 80–140 c µ In most of them an increased amount of bilirubin was shown by the indirect test, and Schumm's test for plasma hæmatin was positive Previous experience showed us that these anæmias always responded to crude liver or to folic acid, and often to oral or intramuscular vitamin B_{12} Some of them had histamine fast achlorhydria, and of these a few, on gastroscopy, had signs of gastric atrophy (Woods 1951) and must therefore be regarded as pernicious anæmia, although they had no nervous involvement or sore tongues

All our patients were kept under observation for three to ten days before receiving any treatment, if their reticulocytes did not increase during this time, they were selected for treatment A positive response to treatment was indicated by an increase in the number of reticulocytes to the maximum for the blood-count in six to twelve days, by a doubling of the blood-count and hæmoglobin in fourteen to twenty one days from the start of treatment, and a change in the marrow from the typical pre treatment megaloblastic type to the characteristic normoblastic erythroblastic picture of normal marrow

Classified according to their response to treatment, there appear to be at least three types of megaloblastic anæmia among Africans

Type 1 responds to penicillin, to oral and intramuscular vitamin B_{12}, to folic acid, and to liver

Type 2 does not respond to penicillin or to oral vitamin B_{12}, but still responds to intramuscular vitamin B_{12} and to liver

Type 3 responds only to folic acid or to crude liver

Clinically and hæmatologically we could not see any difference between those cases which responded to penicillin and those which did not.

Up to now we have treated 24 cases of megaloblastic anæmia with penicillin Of these, 16 gave typical and specific responses 4 did not respond to either penicillin or oral vitamin B_{12} but did respond to intramuscular vitamin B_{12}, and 4 did not respond to penicillin or to either oral or intramuscular vitamin B_{12} but did respond to oral folic acid

Representative Case records

TYPE 1

Double Response to Oral Penicillin

Case 1 (fig 1).—A female Kikuyu aged 24 well nourished and of good physique entered hospital on March 24, 1952, complaining of weakness dyspnœa and pains all over the body She had given birth on March 6 to a child whom she was breast-feeding, and in the usual African way she continued to do so throughout her stay in hospital She said that she had become ill during the last month of her pregnancy

On examination her spleen was enlarged to the umbilicus, her liver was not palpable and she had slight œdema of her ankles her tongue nails, teeth, and nervous system were normal Her lungs and heart showed nothing that was not compatible with her extreme anæmia. Her temperature was 100 F and she had a slight cough

Blood examination on March 25 1952 showed: red cells 845,000 per c.mm; Hb 2·8 g per 100 ml; M.C.V 118 c.μ; mean corpuscular Hb (M.C.H.) 33 μμg mean corpuscular Hb concentration (M.C.H.C.) 28% bilirubin (indirect) 3 mg per 100 ml white cells 2140 per c.mm. no sickling no malaria parasites Kahn test negative

Sternal puncture (March 25 1952) showed an active marrow, with intermediate megaloblasts and giant stab-cells.

Gastric test normal after histamine 1 mg

Treatment and progress.—The patient was kept under observation from March 24 to March 27 1952 during which time her reticulocytes never increased beyond 0·7% From March 28 to March 31 she was given oral penicillin 200,000 units daily By March 31 her reticulocytes had increased to 32%. On April 2 blood examination showed red cells 1 000 000 per c.mm., Hb 3·8 g per 100 ml and M.C.V 135 c.μ During the following eleven days the reticulocytes decreased to 1% On April 3 diarrhœa developed, which was cleared with kaolin As the red-cell count on April 14 was still only 1 430 000 per c.mm the Hb was 4·8 g per 100 ml and the marrow still contained some intermediate megaloblasts, another course of oral penicillin 200 000 units, was given from April 14 to April 22 By April 20 the reticulocytes increased to 20% On May 6 1952 the patient left hospital with a red cell count of 2 000 000 per c.mm. Hb 9 g per 100 ml and a normal bone marrow

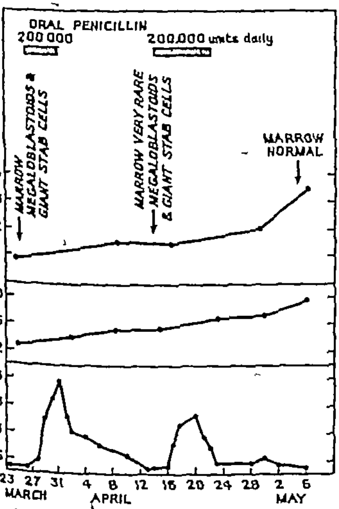

Fig 1—Type-I anæmia showing double response to oral penicillin (case 1)

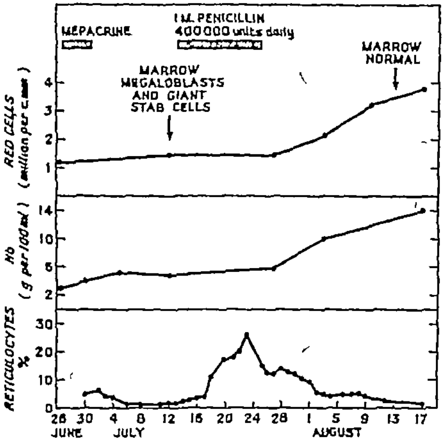

Fig 2—Type-I anæmia showing response to intramuscular penicillin (case 2)

Response to Intramuscular Penicillin

Case 2 (fig 2).—A male Mkamba student aged 19 well nourished and of good physique, entered hospital on June 25 1952, complaining of headache abdominal pain, diarrhœa, and weakness.

On examination his temperature was 103°F spleen 2 (Hackett) and liver palpable and tender His tongue teeth, nails, and central nervous system were normal His red cells were 1 160 000 per c.mm and Hb 2·8 g per 100 ml Falciparum rings were present so a five-day course of mepacrine was given. On recovery from malaria he was found to be severely anæmic and was referred to us on June 30; he was kept under observation, without treatment until July 12.

Blood examination on July 12 showed red cells 1 340 000 per c.mm. Hb 3·8 g per 100 ml; M.C.V 88 c.μ. M.C.H. 33 μμg M.C.H.C 31·4% white cells 3100 per c.mm. bilirubin (indirect) 1·1 mg per 100 ml.; Schumm's test +++ no sickling; no malaria and Kahn's test negative

Marrow puncture on July 12 showed great activity with many typical megaloblasts, intermediate megaloblasts, and giant stab-cells.

Stools contained no ova or cysts

Gastric test normal after histamine 1 mg

Progress and treatment.—While the patient was under observation the reticulocytes decreased from 6·0 to 0·2% From July 13 to July 25 he was given intramuscular penicillin 400 000 units daily His reticulocytes reached 24% on July 23, and on Aug 3 his red cells were 2,100 000 per c.mm. and Hb 9·6 g per 100 ml The patient left hospital at his own request on Aug 17 1952 with a red-cell count of 3,800 000 per c.mm and Hb 12·5 g per 100 ml. marrow still very active erythroblastic normoblastic in character but no megaloblasts.

TYPE 2

Response to Intramuscular Vitamin B_{12} Only

Case 3 (fig 3).—A female Kikuyu aged 32, under our observation since November 1950 had during this period four relapses of anæmia. She always had histamine-fast achlorhydria with no pepsin, and well-marked atrophic gastritis, and apart from the absence of nervous symptoms and glossitis was

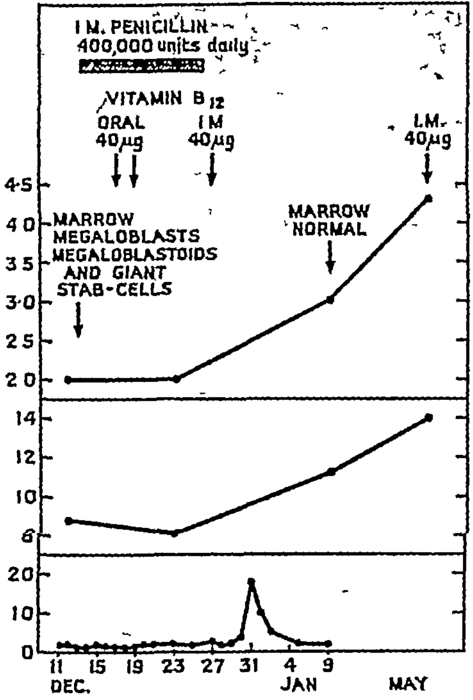

Fig 3—Type-2 anæmia showing response to intramuscular vitamin B_{12} only (case 3)

a typical case of pernicious anæmia. During the first two relapses she was successfully treated with 'Anahæmin' Her third relapse was treated with 80 µg of intramuscular vitamin B_{12}, to which she responded normally Her fourth relapse, which has been fully reported previously (Foy et al. 1952c, case 4), was treated with large doses of penicillin, and at that time we attributed the lack of response to this high dosage. We therefore treated her at the next and fifth relapse with intramuscular penicillin 400 000 units daily

Fifth relapse—She was admitted to hospital on Dec. 11, 1952, complaining of headache, weakness, and palpitations. Her teeth, tongue, nails, and nervous system were normal; she had no œdema, her spleen and liver were not palpable, and her heart and lungs were normal As on previous occasions she was her usual well nourished self

Blood examination on Dec 12, showed red cells 1,960,000 per c.mm., Hb 8 7 g per 100 ml, M.C.V. 122 c µ, M.C.H. 44 µµg, M.C.H.C. 36%, white cells 3020 per c mm., bilirubin (indirect) 3 mg per 100 ml, Schumm's test + + +, no malaria, no sickling and Kahn's test negative

Marrow biopsy showed an active marrow with intermediate megaloblasts, typical megaloblasts, and giant stab cells.

Stools contained no ova or cysts.

Gastroscopy (Dr G C Dockeray) on Jan 3, 1953, showed a pale mucosa with well marked gastric atrophy

Treatment and progress—As the patient had been in our care before, we kept under observation from Dec. 11 to Dec. 13, during which time her reticulocytes showed no variation. From Dec 13 to Dec. 26 penicillin 400,000 i.u. was given daily. On the sixth and seventh days after the start of the course of penicillin she was given 40 µg of vi B_{12} by mouth daily. There was no response to either drug. On Dec. 27 she was given 20 µg only of intramuscular vitamin B_{12}, five days later her reticulocytes increased 19%. She left hospital on Jan 19, 1953, with red cell 2,930,000 per c mm., Hb 11 g per 100 ml, and a normal marrow She visited us on May 8, 1953, with red cells 4,260,0 per c.mm and Hb 14 g. per 100 ml.

Hæmatologically and gastrically the patient appear to be a typical case of pernicious anæmia, and is o interest in that she never responded at any time either to oral vitamin B_{12} or to penicillin, and we believe that the failure to respond was due to complete absence of intrinsic factor, related to her constant and extensive atrophic gastritis and histamine-fast achlorhydria, in contrast to case 4.

Response to Intramuscular Vitamin B_{12}

Case 4 (fig 4)—A female Kikuyu, under our observation since 1949, had six relapses of anæmia.

The *first and second relapses* were successfully treated with 'Neohepatex' in a local dispensary

The *third relapse* was treated with 'Marmite', but, as the patient during this relapse developed pneumonia and was given penicillin, it was difficult to say whether the marmite or the penicillin, or the combination, had produced the remission. At this stage the patient was hypochlorhydric after 1 mg of histamine

The *fourth relapse*, in November, 1950, was successfully treated with intramuscular penicillin alone, and the patient was discharged well, with red cells 4,800,000 per c.mm., Hb 11 g. per 100 ml., and a normal marrow This fourth relapse has been fully described (Foy et al. 1951)

The *fifth relapse* was in September, 1952, when she entered hospital complaining of her usual symptoms, headache, dyspnœa, weakness, low grade pyrexia, and icterus. Her tongue was red at the edges but otherwise normal. Her spleen and liver were not palpable; her teeth, nails, nervous system, heart, and lungs were normal, and she was her usual very well nourished self

Sternal puncture showed active marrow, with intermediate megaloblasts, typical pernicious anæmia megaloblasts, and giant stab cells.

Stools contained no ova or parasites

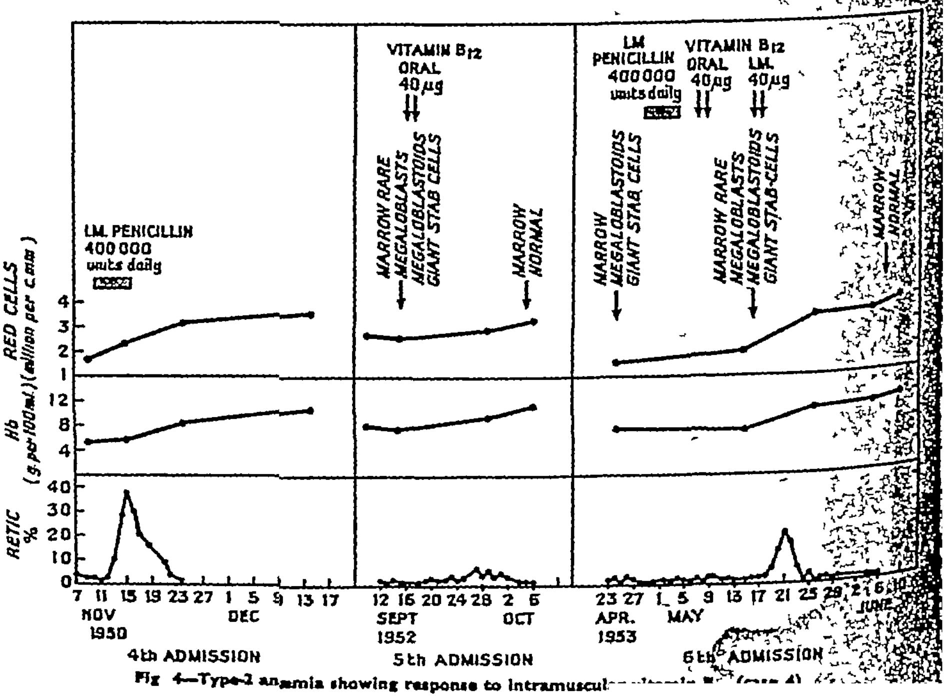

Fig 4—Type-2 anæmia showing response to intramuscul[illegible] (case 4)

Gastroscopy (Dr G C Dockeray) on Oct. 1, 1952 showed a rather anæmic mucosa, which was atrophic and near the fundus slightly greenish grey with prominent blood vessels showing through the mucosa. There was no evidence of erosion or other abnormality. Complete histamine-fast achlorhydria was present.

Blood examination on Sept 15, 1952, showed red cells 2,510 000 per c mm. Hb 8·5 g per 100 ml.; M.C.V. 100 c.µ; M.C.H. 31 µµg, M.C.H.C. 34%; white cells 3000 per c.mm; bilirubin (indirect) 5 mg per 100 ml. Schumm's test ++; no sickling, no malaria, and Kahn's test negative.

Treatment and progress.—The patient was kept under observation from Sept. 11 to Sept. 16, 1952, during which time her reticulocytes varied from 0·7 to 1%. On Sept. 16 and 17 she was given oral vitamin B_{12} 40 µg daily; her reticulocytes showed a submaximal rise to 6%. On Sept 29, 1952, 14 days after the start of this treatment, her red cells were 2 010 000 per c.mm. and Hb 9·5 g per 100 ml. She left hospital at her own request on Oct 7 with red cells 3 140,000 per c mm. Hb 11·6 g per 100 ml., and normal marrow. On Jan. 15 1953 her red cells were 3 910,000 per c.mm. and Hb 13 g per 100 ml.

Sixth relapse.—From October, 1952 to April 1953 she had no treatment and she re-entered the hospital on April 22 complaining of her old symptoms.

Blood examination on April 24, 1953, showed red cells 2,075 000 per c.mm. Hb 8·8 g per 100 ml; M.C.V. 120 c µ; reticulocytes 1·4%; M.C.H. 42·5 µµg; M.C.H.C. 35%; white cells 2000 per c.mm; bilirubin (indirect) 3·5 mg per 100 ml.; and Schumm's test +++.

Sternal puncture on April 24 showed moderate activity of the marrow with many intermediate megaloblasts and giant stab-cells.

Gastroscopy showed very much more conspicuous anæmia of the mucosa and more extensive atrophic gastritis than on the previous occasion, and histamine-fast achlorhydria.

Treatment and progress.—The patient was kept under observation from April 23 to April 28; her reticulocytes showed no change. She was given intramuscular penicillin 400 000 units daily from April 28 to May 4. There was no reticulocyte response or increase of red cells or of Hb. On May 7 and 8 she was given vitamin B_{12} 40 µg by mouth daily; there was no response whatever in the reticulocytes, red cells, or Hb. On May 15 her marrow had typical megaloblasts, as well as the intermediate forms and giant stab-cells found previously. On May 16 and 17 she was given intramuscular vitamin B_{12} 40 µg daily; six days later her reticulocytes had increased to 20%. Ten days after the start of treatment with intramuscular vitamin B_{12} the red cells were 2,912 000 per c.mm and Hb 10·4 g per 100 ml. Nineteen days later, on June 4, the red cells were 3 340 000 per c.mm. and Hb 10·6 g per 100 ml. The patient left hospital on June 12 with red cells 3 010,000 per c.mm. Hb 11·6 g per 100 ml. and normal marrow.

As in case 3 this patient appears, both from the hæmatological and gastric examinations, to have pernicious anæmia. She differs however from case 3 in that she did respond during her early relapses to intramuscular penicillin as well as to vitamin B_{12} 80 µg by mouth. At this stage the atrophic gastritis was not so extensive as in case 3, and she had some free acid in her gastric juice. During subsequent relapses she did not respond to either intramuscular *penicillin or oral vitamin B_{12}, but did* respond to intramuscular vitamin B_{12} 80 µg. We think that this change in response was connected with an increase in both the achylia gastrica and the atrophic gastritis, which in turn was no doubt related to a decrease in the amount of intrinsic factor.

TYPE 3

Response to Folic Acid Only

Case 5 (fig 5).—A female Jaluo aged 30 with a suckling baby aged 1 month whom she continued to feed throughout her stay in hospital, entered hospital on May 19 1953 complaining of weakness, dyspnœa, and headache.

On examination she was a well nourished woman of good physique, without any enlargement of liver or spleen. Her heart, lungs, tongue, nails, teeth, and central nervous system were normal. She said that her illness started during the last two months of her pregnancy.

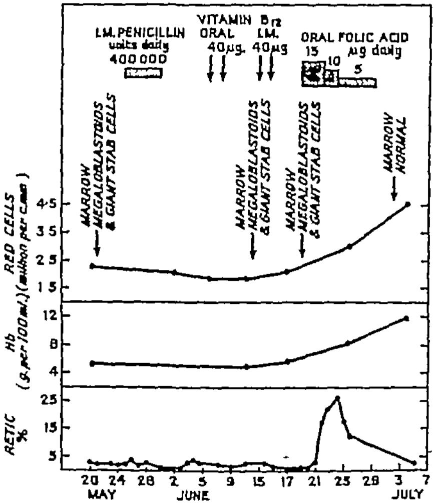

Fig 5—Type-3 anæmia showing response to folic acid only (case 5).

Blood examination on May 20 showed red cells 2,284 000 per c.mm. Hb 5·1 g per 100 ml; reticulocytes 2%; M.C.V. 70 c.µ; M.C.H. 23 µµg; M.C.H.C. 32%; white cells 3140 per c.mm.; Schumm's test negative; bilirubin (indirect) 1·5 mg per 100 ml. Kahn's test negative; no malaria; and sickling trait present.

Sternal puncture on May 20 showed active marrow with intermediate megaloblasts and giant stab-cells.

Stools contained hookworm and ascaris ova.

Gastric test showed hypochlorhydria after 1 mg of histamine.

Treatment and progress.—The patient was kept under observation from May 19 to May 25 with no treatment, during which time her reticulocytes fluctuated between 1 and 2%. She was given intramuscular penicillin 400 000 units daily from May 25 to May 30. Her reticulocytes during this time fluctuated between 0·1 and 3·5%, but there was no real response; on May 30 the red cells had decreased to 2,030 000 per c.mm. and Hb to 4·9 g. per 100 ml. From May 31 to June 6 no treatment was given, and the reticulocytes fluctuated between 0·1 and 3%. On June 6 and 7 vitamin B_{12} 40 µg was given daily by mouth. The reticulocytes showed some slight improvement but no specific response; the red cells on June 10 had decreased to 1 880 000 per c.mm. and the Hb to 4·8 g per 100 ml. The sternal marrow on June 12 gave the same picture as on May 20, with intermediate megaloblasts and giant stab-cells, and the clinical condition had deteriorated. On June 13 and 14 intramuscular vitamin B_{12} 40 µg was given, but there was no response. On June 17 the red cells were 1 906 000 per c.mm. and Hb 4·8 g per 100 ml. The marrow showed no change, and intermediate megaloblasts and giant stab-cells were still present. She was given 15 mg of oral folic acid on June 19, 20 and 21, 10 mg on June 22 and 23, and 5 mg on June 24 and 25. The reticulocytes increased to 25% six days after the start of treatment. On June 26 the red cells were 2 800 000 per c.mm. and Hb 7·5 g per 100 ml. She made an uneventful recovery and was discharged on July 4 with red cells 4 400 000 per c.mm. Hb 10 g per 100 ml., and normal marrow.

This patient appears to have a folic acid deficiency which did not respond either to penicillin or to oral or intramuscular vitamin B_{12}, again emphasising the existence of a relationship between penicillin and vitamin B_{12}. She had sickle-cell trait, grafted on to megaloblastic anæmia, which responded to the appropriate anæmia treatment.

Case 6 (fig 6)—A male Maragoli, aged 20, entered hospital on Feb 13, 1952, complaining of weakness and œdema of the legs He had been under our care in 1951 for megaloblastic anæmia On that occasion he entered with a red cell count of 850,000 per c mm, was treated with folic acid, and made a complete recovery From 1951 until the present admission he had been quite well until the onset of his present illness ten days before coming to hospital

On examination he was a well nourished man of good physique and no enlargement of liver or spleen, his nails, teeth, tongue, and nervous system were normal His heart had a hæmic murmur and was slightly enlarged, he had a slight cough, but his lungs were clear and his sputum did not contain any tubercle bacilli

Gastroscopy on Feb 21, 1952, showed very anæmic mucosa but *no* sign of atrophic gastritis There was hypochlorhydria after 1 mg of histamine

Blood examination on Feb 16 showed red cells 1,310,000 per c mm, Hb 4 g per 100 ml, M C V 89 c μ, M C H 30 4 μμg, M C H C 35%, white cells 3590 per c.mm, bilirubin (indirect) 1 3 mg per 100 ml, Schumm's test + +, Kahn's test negative, no malaria, and no sickling

Sternal puncture showed very active marrow, with many typical megaloblasts, intermediate megaloblasts, and giant stab cells

Stools contained tænia ova

Treatment and progress—The patient was kept under observation from Feb 13 to Feb 18, 1952, during which time the reticulocytes never increased beyond 0 2% From Feb 16 to Feb 22, he was given *intramuscular penicillin 400,000 units daily* His reticulocytes made no response whatever On Feb 22, his red cells had decreased to 750,000 per c.mm and Hb to 2 4 g per 100 ml On Feb 21 and 22 he was given vitamin B_{12} 40 μg by mouth daily On Feb 23, he had slight epistaxis and, as his clinical condition had considerably deteriorated, was given 500 ml of whole blood on Feb 24 Next day his red cells were 940,000 per c mm. and Hb 3 2 g per 100 ml His reticulocytes made no response and remained at 0 2% Marrow puncture on Feb 23, still showed typical megaloblasts and giant stab cells On Feb 25 and 26 he was given intramuscular vitamin B_{12} 40 μg daily, but there was no *reticulocyte response* On Feb 27, 1952, the red cells had decreased to 730,000 per c mm, Hb to 2 4 g per 100 ml, and white cells to 1300 per c.mm On March 2 the red cells were 880,000 per c mm, the marrow was still megaloblastic, and treatment with folic acid was started On the eighth day from the start of treatment the reticulocytes had increased to 34% On March 9, the red cells were 2,030,000 per c mm and there was great clinical improvement The marrow on March 8, 1952, showed complete absence of megaloblasts and giant stab cells The patient was discharged from hospital on March 26, 1952, at his own request with a red cell count of 3,220,000 per c mm and Hb 10 4 g per 100 ml

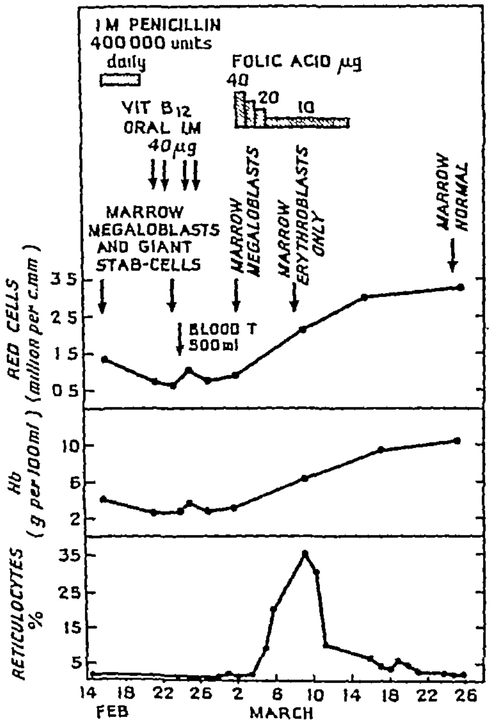

Fig 6—T anæmia showing response to folic acid only (case 6)

This is another example of folic acid deficiency, as in case 5, with no response either to penicillin or to oral or intramuscular vitamin B_{12} A 500 ml transfusion in this case was unavoidable because of the rapid and serious deterioration that took place, but it is well known that small transfusions do not influence reticulocytes or the cytological structure of the marrow

Discussion

It is evident from the above cases that the megaloblastic anæmias of Africans differ in their responses to treatment, as has been found in India and elsewhere The great majority of them respond to penicillin, and a small number do not respond to either penicillin or oral vitamin B_{12} but do respond to intramuscular vitamin B_{12}. Another group respond only to folic acid Those which respond to penicillin or to vitamin B_{12} appear to be deficient in vitamin B_{12} Those that do not respond to penicillin or to vitamin B_{12} but respond only to folic acid are deficient in this substance or its metabolites

The response of type 1 anæmias to penicillin, and the lack of response in type-3 anæmias either to penicillin or to vitamin B_{12} in any form and their subsequent response to oral folic acid, may indicate that penicillin affects the synthesis, metabolism, or absorption of vitamin B_{12} and not folic acid, at least in man

Further, it appears from the lack of response to penicillin and oral vitamin B_{12} in the type 2 anæmias, and their subsequent response to intramuscular vitamin B_{12}, that penicillin influences the biosynthesis and utilisation of intestinal vitamin B_{12}, and, like oral vitamin B_{12}, it is inactive unless intrinsic factor is present

In case 4 (type 2 anæmia) the early relapses responded to penicillin and oral vitamin B_{12}, later, with an increase in the extent of atrophic gastritis, development of complete achlorhydria, and increasing absence of intrinsic factor, no response could be obtained to either penicillin or oral B_{12}, but intramuscular B_{12} was still active

The megaloblastic anæmia accompanying infection with diphyllobothrium behaves in the same way, sometimes responding to oral vitamin B_{12} and sometimes not, and Bonsdorff (1952) suggests that the variation in response is due to changes in the amount of intrinsic factor present.

Penicillin itself contains no vitamin B_{12}, if it did, one would expect it to produce remissions in pernicious anæmia when given by injection, but from the cases described here it is apparent that it does not

We believe that penicillin produces responses in the megaloblastic anæmias of Africans by causing ecological and/or physiological changes in the flora of the gut

The intestinal flora of man and other animals synthesises a wide range of essential metabolites, such as vitamin B_{12}, riboflavine, nicotinic acid, folic acid, inositol, tocopherol, &c, and most of the available evidence *indicates that part at least of these* synthesised products can be absorbed and utilised by the host Indeed, it would be strange if the water soluble vitamins of the B group that are produced by the activities of intestinal micro organisms were not absorbed There is no doubt that vitamin K, for example, produced by the gut flora, is absorbed and made use of by the host in many kinds of animals

An enormous volume of work has been done showing that oral antibiotics increase growth-rates in many different kinds of animals over and above that produced by vitamin B_{12} alone It has also been shown that injected antibiotics cause similar acceleration of growth. Abrahams et al. (1941) found that injected penicillin was excreted in the bile into the gut. Larsen and Carpenter (1952) state that injected aureomycin is present in the fæces of pigs in amounts that vary from 42 μg to 6500 μg per g of dry fæces, and aureomycin given by mouth in amounts from 31 μg to 11 500 μg Elam et al. (1953) have shown that injected penicillin is as effective as oral penicillin in promoting growth It therefore seems that the fæcal concentration and the effectiveness of oral and injected antibiotics are similar and both are sufficient to produce changes in the floral equilibrium accompanied by alterations in synthesis and utilisation of essential metabolites Cuthbertson (1952) has shown that oral penicillin decreases the need for vitamin B_{12} in chicks, and it is not unlikely that when injected it would do the same.

Coates (1953) has suggested that the increased growth may be due to the suppression of some unidentifiable infection which the antibiotic clears. The megaloblastic anæmias with which we have dealt have never had any known pathological infection and the response of these anæmias to penicillin is exactly the same as we get with liver vitamin B_{12}, and folic acid and so far as we are aware these hæmatinics are not thought to produce their effects by suppressing infections but by supplying some hæmopoietic deficiency

The fact that antibiotics often produce resistant and dependent strains of organisms is evidence that profound physiological changes have taken place which may not be reflected by any quantitative changes in the flora. Microbiological evidence indicates that even small changes in the flora in one group of organisms, may be followed by profound alterations in the ecological balance of the whole gut

The view that antibiotics produce their effects by altering the floral milieu of the gut is also supported by the fact that a number of substances which differ from each other and have in common only their bacteriostatic or bactericidal properties—e.g sulphonamides sodium arsanilate cation-exchange resins, and some detergents—can hasten the rate of growth in animals. The common denominator of all these substances is their effect on bacteria, on the medium in which they exist, or on the metabolism of the host (Card 1951)

The biosynthesis and availability of vitamins differ in the different animal species, and the presence of any particular vitamin in the intestinal tract of one species is not evidence of its presence or availability in another Further the responses of the different animal species to antibiotic supplements is not the same, and it is therefore impossible to assume that because an antibiotic has a given effect in one species it will have the same effect in a different species.

The work on germ free chicks (Reyniers et al 1950) was initially interpreted as evidence that changes in intestinal flora were not a factor in the promotion of growth that followed the giving of antibiotics to animals. The work of Luckey (1952) seems to indicate that in the chick at least intestinal flora may retard growth since sterile chicks grow better than non-sterile, and non-sterile ones given antibiotics better than non-sterile ones without antibiotics. Liver damage in rats on a necrogenic diet affects the left lobe and can be prevented by antibiotics; the portal supply to this lobe is from the lower gut, a locus of bacterial activity, and antibiotics may produce their effects in such cases by suppressing flora producing toxins.

Variations in diet are also known to produce great changes in the gut flora dextrin, for example encourages a denser flora than sucrose and rancid fats have a profound effect on the ecology and metabolism of intestinal micro-organisms and have been suggested as a factor in the production of the sprue syndrome The prevalence of megaloblastic anæmia in primitive communities may be connected with a diet predominantly high in bulky carbohydrates and low in first-class protein, which may encourage a flora inimical to the production of essential metabolites.

Antibiotics may bring about their effects by any or all of the following mechanisms:

(1) Ecological changes in the gut flora which lead to the destruction of antagonists or of competitors interfering with synthesis, absorption or utilisation of hæmopoietic factors, or to an increase in those types concerned with the synthesis of vitamin B_{12} or of other hæmopoietic substances.

(2) Interference with bacterial metabolism leading to release or to increase in availability of factors essential either to the host or to other bacteria.

(3) Sparing action of the antibiotic on vitamin B_{12} or on proteins, or effects on amino-acid metabolism or methyl group synthesis.

(4) Destruction of toxins inhibiting hæmopoiesis, or growth of synthesising flora.

(5) Presence in the antibiotic of hitherto unknown hæmopoietic factors.

(6) Changes in metabolism of the host, leading to increased utilisation or absorption of essential factors.

Summary

The megaloblastic anæmias of Africans are of three well defined types, which can be classified according to their response to treatment

Type 1 responds to penicillin and all known hæmatinics

Type 2 does not respond to penicillin or to oral vitamin B_{12} but does respond to intramuscular vitamin B_{12}

Type 3 responds only to folic acid

On the basis of the results described it is suggested that penicillin is in some way connected with the intestinal production of vitamin B_{12}

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PREVENTION OF FERTILISATION BY A HYALURONIDASE INHIBITOR

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The mass of cumulus cells which surrounds the newly ovulated egg in certain mammals, notably the rabbit, was observed to disintegrate rapidly in the presence of spermatozoal suspensions (Yamane 1930 Pincus and Enzmann 1935) The responsible agent was later identified as hyaluronidase the already known 'spreading factor of testis extracts (McClean and Rowlands 1942) These workers all held the view that the adherent cumulus cells must be removed before a spermatozoon could approach and penetrate the zona pellucida, the implication being that a bulk supply of hyaluronidase was required at the site of fertilisation This idea was of interest in that it provided a reason for the production of such vast numbers of spermatozoa by the male mammal and it suggested that human cases of infertility associated with low sperm counts might be assisted by the provision of additional hyaluronidase Some experimental evidence in support of the idea was obtained (Rowlands 1944), but in the course of time several serious objections appeared. In particular, further work (Austin 1948) confirmed earlier observations that usually very few spermatozoa are present at the site of fertilisation, and that fertilisation normally takes place in the rat while the egg is surrounded by cumulus cells (Austin and Smiles 1948) and in the rabbit while the corona radiata is still present (Swyer 1947a) Moreover, renewed attempts to potentiate small numbers of spermatozoa by the simultaneous insemination of additional hyaluronidase gave negative results (Chang 1950)

It has thus become difficult to accept the idea that a bulk supply of hyaluronidase, coming from a mass of spermatozoa, is an essential prerequisite of fertilisation Nevertheless, as Austin has pointed out, a possibility, perhaps a probability, remains that the approach of a spermatozoon to the zona pellucida is assisted by its own individual supply of the enzyme, which may thus have some role in fertilisation in some species It was rational, therefore, to investigate the effect of decreasing the effective availability of the enzyme, by adding either hyaluronic acid complexes or hyaluronidase inhibitors to the semen before insemination, and the addition of hyaluronic acid derivatives (Pincus, Pirie, and Chang 1948) or phosphorylated hesperidin (Chang and Pincus 1953) has been reported to lower the fertilisation-rate in rabbits It should be noted, however, that Chang and Pincus did not get complete inhibition even when the inhibitor was present at a concentration of 1% In view of this, the earlier reports of decreased fertility in rats (Martin and Beiler 1952) and mice (Sieve 1952) following systemic administration of phosphorylated hesperidin, can be regarded as only suggestive, while the startling claim of clinical effectiveness (Sieve 1952) cannot be accepted without confirmation

Quite apart from any question of application to contraception, the work on the effect of inhibitors is a means of investigating the rôle of hyaluronidase in fertilisation, and perhaps that of other enzymes since the hyaluronidase inhibitors commonly used are far from specific I report here the results of an extensive series of experiments on rabbits carried out with a new and powerful inhibitor 'Rehibin'—tri gentisic acid, Compound 21P (Hahn and Frank 1953)—prepared by the research laboratory of AB Ferrosan

Investigations

TECHNIQUE

Rabbit semen was obtained by the use of an artificial vagina (Macirone and Walton 1938) All the inseminations involved in any one experiment, usually 3-6, were made with aliquot parts of a large composite batch The dose for one insemination consisted of 0 25 ml semen plus 0 75 ml Baker diluent (or in special cases 0 75 ml of a source of additional hyaluronidase), plus 1 0 ml Baker diluent containing the required amount of inhibitor The total volume of 2 0 ml was found to be a convenient amount for insemination The female rabbits were given 50 I U chorionic gonadotrophin immediately before insemination to cause ovulation, and they were killed approximately forty eight hours later, by which time fertilised eggs had reached the morula stage

The rehibin was somewhat insoluble in the diluent and the addition of a small amount of alkali (NaOH) followed by neutralisation, was necessary Subsequent experience showed that the water-soluble sulphonic acid polymers, described by Rogers and Spensley (1953), are about equally effective in inhibiting fertilisation and are much more [illegible]venient to work with

ANTI-FERTILISATION EFFECT OF REHIBIN

In preliminary experiments, a wide range of doses of rehibin (25 0–0 1 mg) was tried and the mixture was allowed to stand for one hour before insemination Results indicated that about 1 0 mg was the critical amount, and, in all, only 7 eggs were fertilised out of 45 eggs recovered from 8 rabbits following insemination with semen containing 1 mg of rehibin (table I) This result, obtained with rehibin at a concentration of 0 05%, appears to be similar to that obtained by Pincus and Chang with phosphorylated hesperidin at a concentration twenty times greater It is not evident, however, from my work or from theirs, whether concentration or absolute amount of the inhibitor is the operative factor It may be noted that 25 mg of rehibin in 2 ml of diluted semen had no obvious spermicidal action even after the mixture had been allowed to stand for one hour

RELATION BETWEEN DOSE AND EFFECT

An attempt was then made to determine more accurately the relation between dose and effect over the critical range For this purpose the technique was altered slightly in that the mixture was inseminated immediately without being allowed to stand at room temperature In this experiment three replications were made of a series in which doses of 0 5 mg , 1 0 mg , and 2 0 mg were each used on one rabbit Allowing for the fact that the mixed batches of semen used in each replication may well have varied in hyaluronidase content, the results are remarkably uniform, and indicate a relation between dose and response unexpectedly sharp for this kind of multiple reaction The other interesting feature of these results is that comparison of tables I and II suggests that allowing the mixture to stand before insemination has little effect on the result, so that the action of rehibin, whatever it may be, appears to be rapid.

TABLE I—EFFECT OF ADDING DIFFERENT AMOUNTS OF REHIBIN TO A CONSTANT AMOUNT OF SEMEN (0 25 ML.) (SEE TEXT FOR DETAILS OF TECHNIQUE)

Amount of rehibin added (mg)	No of rabbits	Total no of eggs	Number fertilised
25	1	5	0
10	3	26	0
5	1	5	0
4	2	13	0
1	8	45	7
0 5	1	3	3
0 25	1	7	7
0 1	1	4	4

MECHANISM OF THE REHIBIN EFFECT

An experiment was then carried out in which three different amounts of semen were associated with two different amounts of rehibin, the total volume of the mixture for insemination being kept to 2 0 ml (table III) It will be seen that increasing the amount of semen above 0 25 ml overcomes the effect of 1 0 mg of rehibin, but that the addition of large excess of rehibin in turn "neutralises" even 1 0 ml of semen It seems possible, therefore, in a rough way, to titrate semen against the

TABLE II—DOSE EFFECT RELATION BETWEEN AMOUNT OF REHIBIN ADDED TO 0 25 ML SEMEN AND THE NUMBER OF EGGS FERTILISED

Amount of rehibin added (mg)	No of rabbits	Total no of eggs	Number fertilised
0 5	3	25	24
1 0	3	23	5
2 0	3	24	0

TABLE III—EFFECT OF VARYING THE AMOUNTS OF BOTH SEMEN AND REHIBIN

Amount of semen (ml.)	Amount of rehibin	
	1·0 mg	10·0 mg.
0 25	0/7	0/7
0·5	8/8	0/6
1·0	6 6	0/7

Figures indicate proportion of eggs fertilised One rabbit for each combination.

inhibitor, within a constant total volume of mixture. This result provided further evidence that the effect of rehibin was *more than a non-specific spermicidal action* Further experiments were therefore undertaken in which additional hyaluronidase was added to a mixture containing the usual amount of semen (0 25 ml) and a fully effective dose of rehibin (2·0 mg)

The first source of additional hyaluronidase tried was a freeze-dried extract of bull testis which unfortunately proved to be toxic to the spermatozoa. It was then decided to use rabbit semen without living spermatozoa, as the source of additional hyaluronidase No positive results were obtained with a seven year old freeze dried mixture. Fresh semen in which the spermatozoa had been killed by freezing and thawing was then used, it being expected that the spermatozoa killed by this method would liberate rapidly the store of hyaluronidase, which seeps out of the living spermatozoa rather slowly (Swyer 1947b) Later seminal plasma obtained from frozen and thawed semen by centrifugation was used as the source of hyaluronidase.

In these experiments, therefore, the mixture inseminated consisted of 0 25 ml semen, 0 75 ml. killed semen or seminal plasma, and 1·00 ml. Baker solution containing 2 0 mg rehibin. Table II suggests that this amount of additional seminal hyaluronidase should overcome the effects of 2 mg rehibin but without much margin In practice, 38 eggs were fertilised out of 40 obtained from 7 rabbits inseminated with the mixture This result gave further support to the idea that the effect of rehibin depends on the inactivation of spermatozoal hyaluronidase or other enzyme playing a part in fertilisation.

PRIOR INSEMINATION OF REHIBIN

9 experiments in which rehibin in amounts up to 10 mg., was inseminated one hour before the insemination f semen or normal mating gave no significant positive esults.

SYSTEMIC ADMINISTRATION OF REHIBIN

In view of earlier claims to have inhibited fertilisation by the oral administration of hyaluronidase inhibitors, a arge number of experiments were made giving rehibin by mouth. Rabbits quite readily drank water to which he substance had been added and up to 250 mg per day could be administered by this method. In these xperiments a number of unfertilised eggs were recovered following *insemination or mating of animals so treated,* but no reproducible positive results were obtained. This was perhaps not surprising in view of the doubt as to whether such a substance would be absorbed from the gut—a doubt increased by the apparent failure to secure absorption following subcutaneous or intraperitoneal injection.

Mechanism of Effect of Rehibin

These experiments show that rehibin inhibits fertilisation when added, in vitro to rabbit semen before insemination at the rate of about 5 mg per ml. They also suggest that the effect is not that of a non-specific spermicide and that it depends on the inhibition of hyaluronidase At first sight this result, like the less quantitative one obtained with phosphorylated hesperidin by Pincus and Chang, strongly supports the idea that hyaluronidase plays an essential rôle in fertilisation. For reasons given in the introduction, this rôle is almost certainly not the mass dissolution of the cumulus adhering to the egg after ovulation but it could be that of assisting the individual spermatozoon to penetrate between the residual cells. The results of phase-contrast microscopy of eggs whose non fertilisation was associated with the use of rehibin were mainly concordant with this view, in most instances no spermatozoa were observed nearer to the egg than the inner layers of the residual cumulus and signs of activation (discharge of second polar body formation of female pronucleus) were not observed in eggs found to be undivided at a time when segmentation should have been well advanced Sometimes, however especially where the dosage of rehibin had been marginal, *spermatozoa were seen to be embedded in the zona or* even to have got through into the perivitelline space in eggs showing neither segmentation nor even activation The exact significance of this observation cannot be assessed without detailed comparison with control material, but it may be that the spermatozoon is incapacitated by rehibin in some way other than or additional to, the ' neutralisation " of hyaluronidase

Summary

'Rehibin,' a highly active inhibitor of hyaluronidase prevents fertilisation when added in vitro to rabbit semen before insemination, at the rate of about 5 mg per ml of neat semen

Rehibin has no ordinary spermicidal action in the amounts used and the effect on fertilisation probably depends, at least in part, on its capacity to inhibit hyaluronidase. But this may not be the whole explanation

Attempts to inhibit fertilisation by the administration of large amounts of rehibin orally or by injection gave no reproducible positive results, but absorption of this large molecule material may well have been negligible.

My thanks are due to Miss H. M. Bruce for assistance with the work on systemic administration, to Dr Audrey U Smith who carried out the microscopical examinations of the eggs to Dr H. J Rogers and Dr P Spensley for much helpful information, and to Dr G I M Swyer who first called my attention to rehibin. The technical procedures involved were mainly carried out by my assistant Mr F Crisp. The rehibin was kindly supplied by Mr E M. Bavin of Messrs. Smith & Nephew Research.

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We owe the Flying Saucers to airmen, technicians and the like all members of communities that pride themselves on their realism and common sense. It is hard luck on these fellows, of course. Just as they are beginning to feel that through science technics and know how they are masters of life, it seems that little blue monsters arrive from outer space to spy on them, behaving in a fashion that apparently makes them feel inferior and *somehow guilty* if we leave all the old nonsense behind, run as fast as we can away from gods and devils, saints and witches, we only arrive at the place where three headed Martians are watching us. In short the old wild dreams of the Unconscious break through. Moved by feelings we refuse to recognise we project uncanny and sinister images against the very sky itself What secret bitterness is in the Cup to which these are the Saucers? —J B. PRIESTLEY *New Statesman* Dec. 5, 1953, p 712.

HIRSCHSPRUNG'S DISEASE WITH ASSOCIATED INTESTINAL HÆMORRHAGE

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Before 1948 the terms " megacolon " and " Hirschsprung's disease " were used synonomously and applied to all cases of segmental or total dilatation of the large intestine in which there was no demonstrable organic lesion These conditions are now separated into two distinct clinical entities, largely as the result of the work of Ehrenpreis (1946), Swenson and Bill (1948), and Swenson, Rheinlander, and Diamond (1949) in America, and, in this country, of Bodian, Stephens, and Ward (1949, 1950), who added an important pathological study to their clinical and radiological findings

Pathology

By " idiopathic megacolon " is meant total dilatation of the large intestine down to the anal sphincter This is in contrast to " Hirschsprung's disease," in which the dilatation is confined to the proximal portion of the large intestine Distally, there is a narrow segment of variable length which acts as a functional obstruction In more than 90% of cases this narrow segment is confined to the rectum and part or all of the sigmoid colon Occasionally the dilated portion, besides involving the whole colon, extends for a variable distance along the small intestine Rarely the narrowed segment is in the middle of the large intestine, in which case the segment proximal to it is dilated, and that distal to it is normal

In Hirschsprung's disease Bodian et al (1949) have amplified the work of Zuelzer and Wilson (1948) and have shown that in the narrowed segment there is a total absence of Auerbach's and Meissner's plexuses, though nerve fibrils (thought to be sympathetic in origin) and interstitial cells are present They concluded that this absence of parasympathetic ganglia was congenital The aganglionic segment cannot dilate and therefore acts as an organic obstruction In idiopathic megacolon the parasympathetic and sympathetic ganglia are normal

Clinical Picture

Hirschsprung's disease is genetically determined. In a patient known to have this condition the chances that a brother is similarly affected are about 1 in 5, whereas the chances that a sister is affected are much smaller (Bodian et al 1951)

The passage of meconium may be delayed for several days, and constipation is a feature from the beginning Occasionally vomiting and abdominal distension shortly after birth lead to the diagnosis of obstruction More often the gaseous abdominal distension is of less acute onset Attacks of subacute obstruction, accompanied by stools that are hard and pellety or soft and ribbon like, are relieved by the passage of flatus in bouts of explosive foul diarrhœa As the disease progresses, the abdomen becomes greatly distended, and visible peristalsis may be seen The effect on general health is variabl Growth is usually inhibited, and in some cases wasting is very severe Because of the obstruction occasioned by the aganglionic segment the rectum distal to the obstruction contains little fæces when examined digitally and may be empty Sigmoidoscopy can be performed and the narrow segment negotiated, but at its proximal end an impenetrable fæcal barrier is reached,

Idiopathic megacolon is a condition in which, although constipation is trouble some from an early age, the passage of meconium is not delayed The constipation yields more readily to aperients, and on examination fæcal masses may be felt in the distended abdomen The rectum shares in the general colonic loading and on digital examination is always full

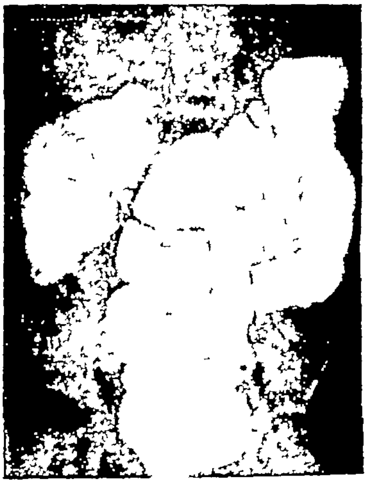

Fig 1—Barium enema in megacolon.

The narrowed segment rendered visible after a barium enema is pathognomonic of Hirschsprung's disease, whereas in idiopathic megacolon the colon and rectum are distended to the anal sphincter (fig 1)

Treatment

Swenson and Bill (1948) were the first surgeons to publish results of rectosigmoidectomy, now extensively practised for the relief of Hirschsprung's disease At first the operation was done in three stages a preliminary transverse colostomy was made and the colon cleared with enemata and washouts , at a second operation the aganglionic segment was removed , and finally, at a third operation, the colostomy was closed Subsequent experience has shown that with careful colonic preparation the operation may be safely completed in a single stage as in the case reported here

Case-Report

A B , aged 2½, is the only child of healthy parents He was born on Dec 15, 1949, by normal delivery after an

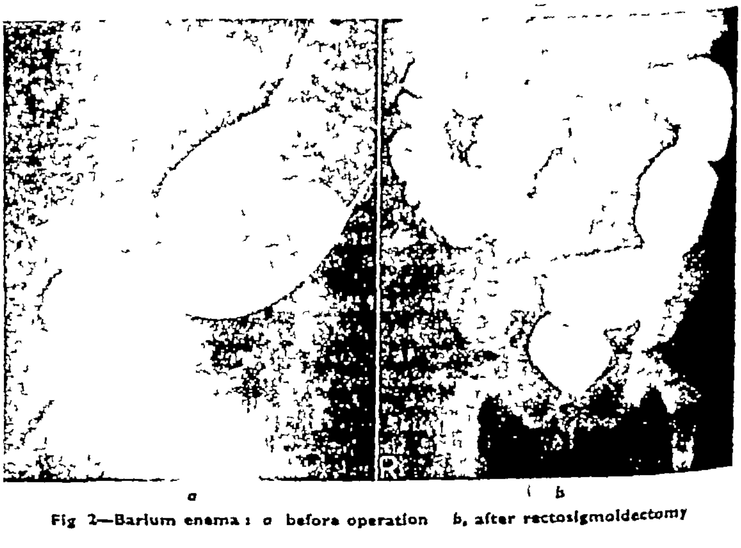

Fig 2—Barium enema : a before operation b, after rectosigmoidectomy

uneventful 30 weeks gestation. At birth he weighed 6½ lb During the neonatal period he had some 'vomiting and constipation,' but no further details are available

History and Investigations

During the first 2 months of life he was seen by Dr L W Hale (to whom we are most grateful for the detailed early history) because of this constipation A barium enema showed a large colon, which was not, however, pathognomonic of Hirschsprung's disease With symptomatic treatment the bowel action became regular The bouts of constipation recurred on several subsequent occasions and necessitated admission to hospital for correction.

In May, 1951 when 17 months old he was admitted because of vomiting pallor abdominal distension, and the passage of blood per rectum. The hæmoglobin was 24% (3·5 g per 100 ml) and the red-cell count 2 100 000 per c.mm The platelets and clotting time were normal. A blood transfusion was given and the constipation again rectified with enemata. Subsequently the fæces persistently gave a strongly positive test for occult blood even when the boy was having voluntary bowel function aided by a combination of liquid paraffin and a high residue diet A barium enema repeated at this time showed megacolon.

The boy was taken home by his parents against advice, but was readmitted 8 or 10 weeks later again with a loaded colon and a hæmoglobin of 38% (5·6 g per 100 ml) His bowel action was corrected and his hæmoglobin raised to 86% (12·7 g per 100 ml) with blood transfusion. Subsequent treatment with large doses of ferrous sulphate did not maintain this level and in a month it had dropped to 75% tests for occult blood in the stools being positive

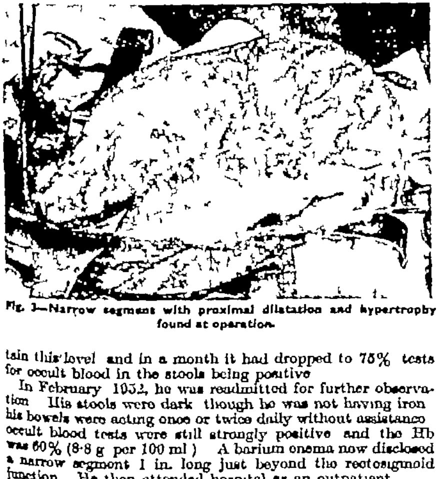

Fig. 3—Narrow segment with proximal dilatation and hypertrophy found at operation.

In February 1952, he was readmitted for further observation His stools were dark though he was not having iron his bowels were acting once or twice daily without assistance occult blood tests were still strongly positive and the Hb was 60% (8·8 g per 100 ml) A barium enema now disclosed a narrow segment 1 in. long just beyond the rectosigmoid junction. He then attended hospital as an outpatient.

In March, 1952, he was readmitted as an abdominal emergency with vomiting constipation, and pyrexia. The acute symptoms rapidly subsided, and investigation showed that the hæmoglobin was 62%, and tests for occult blood in the stools were still positive

On June 20 1952 he was admitted to the Bristol Royal Hospital for Sick Children. He was a well nourished though pale boy weighing 25 lb. 3 oz. (average for age 20 lb) and 33½ in. tall (average for age 33½ in.) Abnormal physical signs were confined to the alimentary system. The abdomen was distended and the colon palpable throughout most of its length A blood-count showed Hb 52% (7·7 g per 100 ml.) white cells 8400 per c.mm. (neutrophils 4200 per c.mm.) and platelets 313 000 per c.mm Tests for occult blood in the stools were negative

On July 12, a barium enema showed the colon to be considerably dilated proximal to a narrow segment at the rectosigmoid junction (fig 2a)

Immediately after admission bowel action was irregular with constipated and occasionally bloodstained stools. Subsequently however all bleeding ceased and further tests for occult blood in the stools were negative Peristalsis was occasionally visible The anæmia was corrected with a blood transfusion, and thereafter the boy was given an oral iron preparation.

On July 18 at sigmoidoscopy the instrument could not be passed beyond the recto-sigmoid junction because of fæcal masses. No cause for rectal bleeding was seen The diagnosis of Hirschsprung's disease being firmly established the patient was prepared for operation

Preparation for Operation

Daily olive oil enemata and later rectal washouts for about 8 weeks reduced the distension of the colon. On Oct. 13 1952 the sigmoidoscopy was repeated under general anæsthesia, and a rectal tube was passed into the colon and fixed in place with strapping Colon washouts were done thrice daily until the rectosigmoidectomy was performed 3 days later

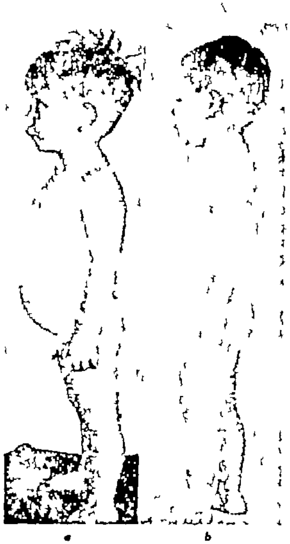

Fig 4—Appearance of abdomen: a before operation; b after rectosigmoidectomy

Rectosigmoidectomy

At operation the great hypertrophy of the colon proximal to the obstruction and the narrow segment were seen at once (fig 3) The operation was done by the 'pull through' technique using two layers of interrupted sutures for the anastomosis. The colon was empty and the success of the preoperative bowel preparation without resort to colostomy was apparent. The resection extended distally to just above the anal sphincters and proximally for 5 in. above the narrow segment

Result

Postoperative course was uneventful. There was no interference with bladder function, and the urethral catheter was removed on the morning after the operation. The bowels were opened daily when he was discharged from hospital and there was no interference with continence He was readmitted 5 months later when he weighed 30½ lb His bowels were now acting normally he had no abdominal distension (fig. 4), and a barium enema showed a normal colon (fig 2b)

Pathology

The muscle wall of the colon and rectum varied in thickness but in one area it narrowed and it was here that no ganglion cells could be seen in either the submucous or the myenteric plexus. In the thickened part of the muscle however ganglion cells were present normally and nerve-fibres were also seen There was no mucosal ulceration

Discussion

Because intestinal hæmorrhage is so unusual in Hirschsprung's disease, this case is worthy of comment.

Until the age of 17 months the symptoms and signs were compatible with Hirschsprung's disease. After this the rectal hæmorrhage was severe enough to reduce the hæmoglobin to 24% (3·5 g per 100 ml) and 38% (5·6 g per 100 ml) on two occasions, suggesting the alternative diagnosis of neoplasm and of angioma of the bowel A barium enema did not disclose any cause for the severe rectal bleeding

Although intestinal bleeding is rare, anæmia is often found in Hirschsprung's disease as a result of chronic ill health and malnutrition Of the 39 children reported by Bodian et al (1949) 4 were moderately anæmic and in 2 others the hæmoglobin dropped to 35% and occult blood was present in the fæces Stammers and Rains (1952) reported a lad, aged 18, in whom the hæmoglobin fell to a similar level (36%), but this was attributed to malnutrition, he was not known to have any frank or occult bleeding from the bowel at any time (Stammers, personal communication). We assume that the severe bleeding in our patient was due to stercoral ulceration secondary to fæcal impaction

Compared to simple idiopathic megacolon with rectal stasis, the incidence of Hirschsprung's disease is small The records have been reviewed at the Bristol Royal Hospital for Sick Children of all patients in 1947–52 diagnosed as having either Hirschsprung's disease or idiopathic megacolon, and where doubt has existed about the correctness of the diagnosis the patient has been re examined, if necessary by barium enema Of the total of 42 patients 35 (83 4%) had simple idiopathic megacolon and 7 (16 6%) had true Hirschsprung's disease

Summary

A case of Hirschsprung's disease is described in which intestinal bleeding (an unusual phenomenon) was a prominent clinical feature The results of rectosigmoidectomy were satisfactory

We are indebted to Prof A V Neale, who referred the case to one of us, for his interest in this paper Dr J M Sheach carried out the radiological investigations, and the department of clinical photography of the University of Bristol provided the photographs

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ACUTE HEPATIC NECROSIS

COMA TREATED WITH SODIUM GLUTAMATE

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GLUTAMIC acid has been used by Walshe (1953) to treat coma due to subacute or chronic liver injury We have recently had a case of acute hepatitis, probably of virus origin, associated with cerebral symptoms, which has responded to such therapy Latner (1950) has reported 5 cases of "acute yellow atrophy" in which the normal modern supportive therapy led to recovery from coma, but no other such cases have been published

Case-record

Miss A, a university student aged 22, had had appendicitis at the [illegible] of 4 There was no history of transfusions or of taking drugs. A possible source of infection was from penicillin injections for boils some three months ago A month before the present illness she had been travelling abroad in Norway, Holland, and elsewhere The Friedman test was negative For two or three weeks before admission she had not been feeling well, had anorexia, and was mildly depressed There was nothing relevant in the family history

Sept 24—Onset of vomiting Took fluids well and was mentally normal

Sept 27—Vomiting persisting and anorexia getting worse Temperature 99°F

Sept 28—Not taking fluids well, and developing a mild icteric tinge

Sept 29—Refused to take anything by mouth and appeared on occasions to lapse into coma Seen by one of us (C E W) and admitted to Scarborough Hospital Then stuporose but attempted when left alone to get out of bed and walk about. Temperature 100–101°F, pulse rate 100 per min Blood pressure 130/85 mm Hg Slight clinical jaundice Respiratory and cardiovascular systems normal No apparent abdominal tenderness No definite liver enlargement and spleen not felt Extensor plantar responses were found during the period of coma, but there were no other abnormal neurological signs

Sept 30—Little change, still mild jaundice, but maniacal symptoms developed, with attacks of screaming when feeding or venepuncture was attempted, followed by coma and stupor Had to be controlled periodically with intramuscular paraldehyde 10 ml

Oct 1—Jaundice deepening and cerebral condition the same Treatment with 10% intravenous glucose and vitamin supplements intravenously and intramuscularly was started Crystalline vitamin B_{12} (cyanocobalamin) 200 µg was given

Oct 2—Both jaundice and coma were deep and there were periods of considerable restlessness Bile present in the urine but no urobilinogen detected. Sodium glutamate therapy was started, and in the following twenty four hours 60 g was given in three doses of 20 g intravenously in 1 5 litres of 10% glucose solution There was no dramatic improvement, but during the absorption of the sodium glutamate the patient was definitely more restless and less comatose She was gravely ill, and the immediate prognosis seemed very poor The lung bases were clear, and there was no œdema Aureomycin 250 mg six hourly was started, and continued via a Ryle's tube until it could be taken orally

Oct 3—Jaundice still deeper, and coma persisting Two doses of sodium glutamate 20 g were given intravenously in 500 ml of 10% glucose at 10 45 A M and 5 30 P M. Two hours after the first dose the patient was slightly less jaundiced but noisy and very restless No urobilinogen Bilirubin present in urine

Oct 4—Less deeply comatose, and jaundice appeared lighter All treatment continued and sodium glutamate 20 g given intravenously Still no clinical fluid retention in the tissues Again there was an increase in restlessness during the absorption of the sodium glutamate

Oct 5—Patient regained consciousness and was soon able to take oral feeds Intravenous drip was discontinued, and glutamic acid 5 g in amorphous powder suspended in 4 oz. of milk was given six hourly, at first by Ryle's tube, but soon by mouth. The mental condition rapidly improved, and in a few hours she was mentally normal. During the coma the fluid balance was well maintained.

Further Progress—From this date the patient has remained mentally clear On Oct 19 jaundice was still present but was clearing Oral glutamic acid 20 g daily in divided doses was continued until Oct 15 Since it was stopped there has been no deterioration in the mental state, which has remained normal. All vitamin supplements and aureomycin therapy are continuing Appetite is good, and apart from its taste the glutamic acid has been well tolerated. There has been no evidence of renal tubular necrosis during the illness.

Pathological Investigations—On admission on Sept 29 the urine showed traces of bilirubin, but urobilinogen was absent A blood-count showed Hb 120%, red cells 5,900,000 per c.mm., colour index 1, leucocytes 7000 per c mm (neutrophils 56%, monocytes 2%, lymphocytes 42%) A stained film showed no significant abnormality Serum agglutination reactions for salmonella organisms were negative. The serum alkaline phosphatase level was 9·6 units per 100 ml., and the thymol turbidity 14 units per 100 ml. The total serum protein level was 7·6 g. (albumin 3·9% globulin 3·7%) per 100 ml. The serum bilirubin level was 12·5 mg per 100 ml The pattern of the electrophoretic filter paper strip (Flynn and de Mayo 1951) showed a qualitative increase in the gamma-globulin fraction. No leptospira were seen in the urine and serum agglutination tests for the leptospiral group were negative.

On Oct. 5 the liver function tests showed no change but the serum bilirubin was reduced to 10 mg per 100 ml and the blood urea was 20 mg per 100 ml. Urobilinogen was found on this day for the first time and has been present since.

Follow up.—On Oct. 21 the *patient was transferred to a* nursing home in Leeds under Dr I Macpherson, who on Nov 24 sent the following report for which we are indebted to him: At present the patient is only slightly jaundiced, and there has been no bile in the urine for at least a week She has received a high protein low fat diet with methionine 1 g t.d.s. vitamins B and C, and Castlan 2 drachms t.d.s. Liver function tests on Nov 18 showed serum alkaline phosphatase, 7 units per 100 ml. serum gold sol no 5 and serum thymol turbidity 10 units per 100 ml It is therefore clear that liver function is still considerably impaired.

Comment

Although it cannot be categorically stated that the sodium glutamate therapy was responsible for recovery in this case we feel that without such treatment the prognosis would have been extremely poor and the result obtained warrants its further trial in hepatic coma Walshe (1953) has proved its value in subacute and chronic liver disease with cerebral manifestations, but we have not been able to trace any reference to its trial in acute hepatic necrosis. Its mode of action is unknown but it does seem to be of value as a supportive measure until the virus invasion can be dealt with by the natural defence mechanisms. The fault in hepatic coma may be a deficiency of glutamic acid (*Lancet* 1953) a substance necessary for removing the toxic ammonium radicle produced as a normal cerebral metabolite which combines with glutamic acid to form the amide glutamine Our dosage of sodium glutamate was far higher than that recommended by Walshe who warns of the danger of water retention due to sodium intoxication We found no evidence of this despite the dosage used, and serum sodium estimations at the end of the intravenous therapy gave a figure just below normal The only effect apparent clinically was to increase restlessness Salivation flushing, and vomiting were not noted at all Our normal procedure was to administer sodium glutamate 20 g in 500 c.cm of 10% glucose allowing three or four hours for the infusion No adverse effects were noted, even when on one occasion by mistake the intravenous dose was administered far too quickly

Although evidence of the value of aureomycin in virus hepatitis is conflicting in view of the severity of the present case we felt that its use was justified especially as recent work has shown that the mortality of experimentally induced acute hepatic necrosis in rats is significantly reduced by this antibiotic The effect may be a direct nutritional one on the liver

We are indebted to Dr J C Broom for undertaking the leptospiral agglutination tests; to Dr I. Macpherson, the Leeds Hospitals, and British Drug Houses Ltd for supplies of sodium glutamate and glutamic acid; to Dr J P Whitehead for help with the pathological investigations and to Mr F B Trenholme for technical assistance.

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BRONCHIAL NEOPLASM WITH MYASTHENIA

PROLONGED APNŒA AFTER ADMINISTRATION OF SUCCINYLCHOLINE

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THE association of bronchial neoplasms with lesions of the central and peripheral nervous system is well known The presence of severe muscle weakness in a case of bronchial neoplasm seen in this hospital in 1951 and its almost immediate disappearance after removal of the tumour, suggested that such neoplasms might give rise to an unusual form of peripheral neuropathy possibly similar to myasthenia gravis When unequivocal features of myasthenia and an abnormal response to succinylcholine were seen in another case of bronchial neoplasm the abnormality of neuromuscular transmission was investigated fully

Case record

A carpenter aged 47 was admitted to St. *Thomas's Hospital* in July 1953, complaining of progressive muscle weakness. He stated that he was well until February 1953, apart from a fall off a ladder in November 1952 as a result of which he suffered a brief period of unconsciousness and a trivial injury to his elbow In February 1953 he noticed that after lunch his legs, from the thigh down became progressively weaker on walking Thus, while he was normal on rising in the mornings, by the evenings he found it difficult to stand. Three weeks after the onset of this weakness he was obliged to give up work Later his arms also became involved, and he found that his head felt heavy while watching television, and he had to support it. At this time he also had transient diplopia on looking to the right and transient difficulty in swallowing towards the end of a meal. There was no nasal *regurgitation. No ptosis or speech defect was complained of* and he had not noticed any abnormality of consciousness memory sensation, or micturition. He smoked 20 cigarettes a day and enjoyed his daily pint of beer

CLINICAL EXAMINATION

He was an alert healthy looking man weighing 60·7 kg His speech was somewhat thick and slurred but he stated that there had been no recent change in it The fundi and cranial nerves were normal. His muscle power was generally weaker than his muscle bulk would suggest, especially the muscles of the shoulder girdle, hip girdle, trunk, and anterior compartments of the legs. Their tone was normal The arm reflexes were diminished The abdominal reflexes were absent and the left ankle jerk was diminished. The plantar reflexes were both flexor All forms of sensation were normal. No excessive fatigability of muscles could be demonstrated The only abnormality observed in the chest was a diminished percussion note on the anterior aspect of the right apex. All other systems were normal on clinical examination.

INVESTIGATIONS

Radiography of the chest showed collapse of the right upper lobe with enlarged right upper hilar and paratracheal glands.

Bronchoscopy (Mr G Kent Harrison) showed a new growth presenting through the posterior wall of the lowest inch of the trachea and involving the right main bronchus.

For this operation the patient was anæsthetised with thiopentone sodium 0·5 g and succinylcholine 50 mg followed by inflation of the lungs with oxygen. Spontaneous respiration did not return until an hour later (normal period of apnœa 2–5 minutes), and the tidal exchange was inadequate until a further 30 minutes had elapsed During this period of apnœa electrodiagnostic examination revealed considerable neuromuscular block, direct muscle stimulation was normal, and there was a double type of intensity duration curve This indicated that the persistence of muscle paralysis was of peripheral origin A sample of blood was taken for determination of cholinesterase and pseudocholinesterase levels

Bronchial Biopsy (Dr J L Pinniger)—Microscopy showed an oat cell carcinoma Culture gave a profuse growth of pneumococci and a few colonies of *Neisseria catarrhalis*

Electrodiagnosis—Several of the weak muscles were examined but showed no significant abnormalities of the intensity duration curves No fibrillation potentials were detected on electromyography Motor-unit action potentials and interference pattern were within normal limits in the affected muscles These findings were regarded as being against a diagnosis of a lesion producing lower motor neurone degeneration.

Cholinesterase Levels (Dr H Lehmann)—Pseudocholinesterase 56 units (normal limits 51–121 units), true cholinesterase 135 units (normal limits 75–150 units)

Liver function Tests—Total protein 6 1% (albumin 3 8%, globulin + fibrinogen 2 3%), thymol turbidity 2 units, alkaline phosphatase 8 5 units

Blood count showed Hb 78%, red cells 3,830,000 per c mm., packed cell volume 33%, mean corpuscular volume 82 c mm., mean corpuscular Hb concentration 33%, white cells 9900 per c.mm (differential count normal), erythrocyte sedimentation rate 122 mm in 1 hour (Westergren)

NEUROMUSCULAR TRANSMISSION

The prolonged apnœa following the administration of succinylcholine and occurring in association with the symptoms of myasthenia and in the presence of normal cholinesterase activity suggested a change in response of the motor end plate to depolarising drugs

Response to Decamethonium—The administration of intravenous decamethonium 2 mg (0 033 mg per kg) to the conscious patient in two separate doses of 1 mg was followed by paralysis of skeletal muscle Respiration became severely embarrassed and had to be assisted Despite the striking loss of volitional activity the action potentials of the hypothenar muscles of the right hand, obtained by supramaximal stimulation of the ulnar nerve at the wrist ten times a second, were maintained Further, a minute after the intravenous injection of 20 mg of ‘Tensilon’ (a short acting neostigmine analogue) respiration returned to normal and the patient opened his eyes and talked freely The recovery of grip strength was less dramatic

This response to decamethonium and its reversal by tensilon are similar to those described for myasthenia gravis (Churchill Davidson and Richardson 1953)

Response to d Tubocurarine—The well known sensitivity of myasthenia muscle was exhibited by this case After the induction of anæsthesia with thiopentone 0 5 mg followed by nitrous oxide and oxygen the intravenous injection of *d*-tubocurarine 3 75 mg (0 0625 mg per kg) led to apnœa lasting 10 minutes, with a further period of 12 minutes during which respirations were of inadequate volume Such a dose of curare would not stop respiratory activity in a normal man of similar physique

Response to Succinylcholine—With the patient similarly anæsthetised, intravenous succinylcholine 7 5 mg (0 125 mg per kg) caused 6 minutes apnœa with a further 4 minutes' inadequate tidal exchange On repetition of this procedure the injection of tensilon 20 mg led to an immediate improvement in respiratory volume

Response to Neostigmine—The patient was given neostigmine sulphate 15 mg by mouth three times a day for two weeks and this improved his hoarseness and skeletal muscle power

Discussion

The association of carcinoma of the bronchus with the symptoms of myasthenia has not previously been reported. In the present case there is strong clinical evidence for believing that the severe muscle weakness is of the myasthenic type, and this belief is supported by the following facts

(1) There is no evidence of any lower motor neurone degenerati

(2) There is increased sensitivity of the skeletal musculature for *d*-tubocurarine

(3) Electromyographic measurements following the intravenous injection of decamethonium were similar to those seen in cases of myasthenia gravis (Churchill Davidson and Richardson 1952)

(4) The neuromuscular block produced by decamethonium and succinylcholine was reversed by tensilon, a neostigmine analogue

(5) Considerable symptomatic improvement followed oral neostigmine therapy

For a clearer understanding of the abnormality of neuromuscular transmission in the present case it is necessary to recapitulate certain features In normal people both decamethonium and succinylcholine act at the neuromuscular junction essentially like acetylcholine they produce an area of depolarisation on the muscle membrane in the region of the motor end plate—i e, depolarisation block This type of block is potentiated by anti cholinesterase substances In contrast, *d*-tubocurarine raises the excitation threshold of the motor end-plate for acetylcholine, leading to a neuromuscular block by competitive inhibition Such a block is rapidly reversed by anti cholinesterase substances

There is, however, a third type of neuromuscular block—described in animals as a “dual mode of response to depolarising agents”—in which the motor end plate first responds by depolarisation followed by a transition to a block of the competitive inhibition type (Zaimis 1952) In myasthenia gravis it has been suggested that the abnormality of neuromuscular transmission is one of altered response of the motor end-plates from depolarisation to the dual mode of action, with the result that the end-plate responds to acetylcholine, decamethonium, and succinylcholine first by depolarisation and then by competitive inhibition (Churchill Davidson and Richardson 1953) Only on such a basis can the response to decamethonium, succinylcholine, and *d*-tubocurarine in the present case be satisfactorily explained, for in each instance a neuromuscular block of the competitive inhibition type resulted, and this was readily reversed by anti cholinesterase drugs

The period of prolonged apnœa that followed the injection of succinylcholine is of great interest Clearly this cannot be explained by a low plasma cholinesterase level, which is the common cause of this condition (Bourne 1953) If it had been possible to distinguish between a low plasma-cholinesterase level and myasthenia during the period of apnœa, a dose of neostigmine would almost certainly have reversed the paralysis Further, it is interesting to note that three cases of prolonged apnœa after the administration of succinylcholine which dramatically improved on the injection of neostigmine have already been reported (Hamer Hodges 1953, Grant 1952, Ruddell 1952)

There remains, therefore, to be considered the possible relation between carcinoma of the lung and myasthenia. Any views must be entirely speculative, but in the previous case seen at this hospital the removal of the tumour led to a dramatic symptomatic improvement Similarly, cases of myasthenia gravis have been reported in which removal of the thymus and the thyroid glands have been followed by an amelioration of the symptoms. The rôle of the thymus gland in myasthenia remains unknown, but it would be of great interest to know whether this specific change in the reaction of the motor end-plate—myasthenia—occurs in association with other forms of carcinoma

Summary

A case of carcinoma of the lung showing myasthenic weakness is described

Investigations showed that the response of the motor end plate to *d* tubocurarine, decamethonium, and succinylcholine was similar to that seen in myasthenia gravis

The significance of the prolonged apnœa following ccinylcholine is discussed

We wish to thank Dr. H. Lehmann of St Bartholomew's ospital, for the plasma-cholinesterase determinations We knowledge with gratitude that the expenses of this investi tion were borne by a grant from the endowment fund of ; Thomas's Hospital Miss J F Davenport rendered valuable ecretarial assistance

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POLYMYXIN B

AN INTRATHECAL REACTION

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POLYMYXIN B is becoming increasingly recognised as potent bactericidal weapon against certain gram egative organisms. To be effective in meningeal nfections it must be given intrathecally it does not ass the blood brain barrier (Brownlee and Bushby 1948)

Polymyxin B is irritant to tissue especially when njected intramuscularly a pleomorphic reaction in the erebrospinal fluid (C.S.F) has been reported together ith an increase in the meningeal symptoms (Swift and Bushby 1951), but no emphasis has been placed on the ossibility of more severe sequelæ. On the contrary s injection intrathecally has been very recently said to e harmless (Jawetz 1952, *British Medical Journal* 1953)

CASE RECORD

A married woman aged 28 was admitted on Nov 10 1952 ith three days history of malaise, severe occipital headache ausea and vomiting and occasional rigors with aching pains n the limbs. Mild photophobia was noticed. No specific eakness was present and there were no other symptoms. She had had a recent frontal sinus infection for which a ubmucous resection had been advised.

On admission her temperature was 99·4 F pulse-rate 80 espirations 20 a minute, and blood pressure 120/60 mm. Hg She was perfectly conscious, but in considerable distress, with evere neck rigidity and tender occipital and upper dorsal thoracic muscles. Kernig's test was positive at 45 with pain. The right grip was rather weak. No other motor weakness was found. The right knee-jerk was accentuated. Otherwise routine clinical examination revealed no abnormality

Lumbar puncture produced clear C.S.F under a pressure of 125 mm. H_2O which was transmitted normally The C.S.F contained 155 small mononuclear cells per c.mm and protein 40 mg per 100 ml The Wassermann reaction and Lange test were negative.

Progress—On Nov 17 there was increasing weakness in the right arm. The right knee jerk remained accentuated. There were no sensory changes. Catheterisation became necessary because of retention of urine A few colonies of *Bacterium fæcalis-alkaligenes* were at this stage grown in the first specimen of C.S.F On Nov 18 the neck rigidity was slightly increased the right knee jerk was much diminished, and a white cell-count showed 7200 (polymorphs 48-0 lymphocytes 1948 monocytes 144 eosinophils 216) per c.mm. The C.S.F was clear and under normal pressure and contained 165 small mononuclear cells per c.mm., protein 40 mg per 100 ml., and chloride 760 mg per 100 ml. Culture produced a pure growth of an organism identical with that previously isolated On Nov 21 severe headache and vomiting recurred Neck rigidity was still present and there was no change in neurological signs. It was now reasonably certain that the responsible organism was *Bact fæcalis-alkaligenes* Radiography of the spine and skull a high nasal swab and culture of the stools did not help to elucidate the source of the infection. The organism was found to be sensitive only to polymyxin B The patient was deteriorating rapidly with severe headache meningism, and vomiting the ankle-jerks were still present. The fact that the organism had been isolated twice decided us to use polymyxin B

Treatment and Course.—On Nov 22 treatment was begun with polymyxin B (the later or purified type) 100 000 units intrathecally b.d and 250 000 units intramuscularly six hourly Twelve hours after the first intrathecal injection the C.S.F became turbid and the patient more febrile, meningism was much increased. The sites of the intramuscular injections were painful Three intrathecal injections were given twelve hourly but owing to the intense meningeal reaction further administration was stopped. On Nov 24 the C.S.F was cloudy and contained 4000 cells mainly polymorphs per c.mm., and chloride 680 mg per 100 ml. culture was sterile after forty-eight hours. On Nov 25 neck rigidity was severe and there was severe urinary retention The C.S.F was clearer and contained 990 cells (polymorphs 60% small mononuclears 30% large mononuclears 10%) per c.mm Culture was sterile after forty-eight hours. On Dec. 1 the neck rigidity had disappeared but the right ankle jerk was absent and the right knee jerk diminished. Sensation was normal, but there were generalised weakness of the legs and fæcal incontinence in addition to the urinary retention By Dec. 13 a complete cauda-equina lesion had developed with motor weakness, loss of ankle-jerks, a saddle shaped area of anæsthesia, urinary retention and fæcal incontinence The right knee jerk remained diminished and there was much muscular weakness in both legs. The C.S.F on Dec. 8 was clear but contained 191 small mononuclear cells per c.mm, protein 170 mg per 100 ml and chloride 700 mg per 100 ml On Dec. 15 the C.S.F was clear and under a pressure of 70 mm. H_2O transmitted normally It contained 71 small mononuclear cells per c.mm., protein 270 mg per 100 ml chloride 710 mg per 100 ml., and sugar 70 mg per 100 ml In view of the increased amount of protein in the C.S.F and the neurological signs it was considered that a partial arachnoid block was developing Accordingly streptokinase 100 units was given intrathecally in 1 ml of physiological saline solution. The patient was transferred to the West End Hospital for Nervous Diseases under the care of Dr C. Worster Drought. After that her clinical condition gradually improved, and the amount of protein in the C.S.F slowly decreased to such an extent that further intrathecal therapy was not indicated The C.S.F towards the end of January was almost normal containing 2 lymphocytes per c.mm. and protein 45 mg per 100 ml and a white-cell count was normal Two cultures of the C.S.F., one in this hospital and one in the West End Hospital for Nervous Diseases, revealed no acid fast bacilli (culture on Löwenstein medium and animal inoculation)

Follow-up—The patient's present state shows much improvement in power of both the right arm and the legs; she is walking well the right knee-jerk is still diminished, the left has improved both ankle-jerks are still absent, and sensory impairment is still present but of considerably less severity Sphincteric control is satisfactory

DISCUSSION

There is no doubt of the antibacterial effectiveness of polymyxin B A generalised meningeal reaction was produced, and, as it subsided an arachnoiditis affecting the cauda equina became apparent The rapid loss of ankle-jerks soon after intrathecal medication supports the view that this was due to the polymyxin and not to the meningitis.

A transient neurotoxæmia has been reported (Jawetz 1952), but no objective neurological signs were produced The evidence in the present case suggests that the damage is due to more than this.

Since polymyxin B is recognised as an irritant [illegible] injected intramuscularly, caution should [illegible] in using it intrathecally We emphasise that [illegible] is of undoubted value and should be used [illegible] Polymyxin B has been given [illegible] units intrathecally without ill effect There is no history in this patient of drug sensitivity or allergy

We suggest that, when used intrathecally, polymyxin B be given in much greater dilution initially, the concentration being increased rapidly in subsequent injections

SUMMARY

A case of meningitis due to *Bact fæcalis alkaligenes* successfully treated with polymyxin B is recorded

A cauda equina lesion complicated the therapy

A low dosage is advised initially

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Medical Societies

ROYAL SOCIETY OF MEDICINE

Hypothermia and Hibernation

THE section of anæsthetics met on Dec 4, under the chairmanship of Prof R R MACINTOSH, its president, to hear three short papers

ANTI HISTAMINES IN ANÆSTHESIA

Dr A J W BEARD noted that anti-histamine drugs are members of a group which are said to inhibit acetylcholine, adrenaline, and histamine in varying degrees He described three effects of interest to anæsthetists sedative, anti-emetic, and that producing hypothermia The sedative effects differ from those of barbiturates and the experimental evidence for this was described, as were the effects on man He illustrated the sleep prolonging effect of chlorpromazine ('Largactil'), the latest of these drugs, by a film If, Dr Beard said, mammals are curarised or deeply anæsthetised to prevent shivering, the body may be cooled in various ways with consequent reduction in oxygen need so also after anti histamines or more especially chlorpromazine So called "artificial hibernation," an unfortunate term, is produced in France by the "lytic cocktail"—a mixture of chlorpromazine, pethidine, and promethazine ('Phenergan') The blood-pressure falls a little, especially with posture or other agents, thus diminishing bleeding, in his experience the pulse-rate has often risen, especially in the early stages, to levels above 100 per minute Postoperatively, patients often lie quiet and contented and free from pain He has found that administration of the mixture, or of chlorpromazine alone, greatly decreases the quantity of anæsthetic agents—particularly thiopentone—needed later He emphasised how peaceable are the laryngeal and bronchial reflexes, and briefly described applications in thoracic surgery, as well as mentioning uses in vomiting, in severe pain, and in pædiatrics, obstetrics, and cerebral surgery

It is possible that the benefit to anæsthesia from these drugs, and from some newer combinations in use on the Continent, may be due to their sedative and their anti shock properties, which are probably related to their sympathetic-blocking effects This suggestion derives from experimental work, particularly that of Freeman and of Wiggers Dr Beard said that he had tried to provide a background to the subject which would be filled in by the teams who will eventually be publishing their results He thought that while uncritical enthusiasm was unreasonable, so was condemnation without reading the literature or trying the drugs His own feeling was that in some cases, he would now be sorry to be without their help

EXPERIMENTS WITH DEEP HYPOTHERMIA

Dr A A JUVENELLE (Paris) sought to define hypotherm[illegible] cooling of the whole body, as distinct from refri[illegible] which implies part of the body By definition, hypothermia should be reserved for a temperature fall to 25°C, while deep hypothermia should describe temperatures below this In dogs he has maintained life by an artificial circulation, in the presence of ventricular fibrillation, at a very low temperature for up to seven hours After re-warming normal rhythm returns, and recovery is complete in 40% of animals Biochemical changes during hypothermia are similar to those found in hibernating animals and are reversible by rewarming Cold does not prevent tissues from getting oxygen from the blood Dr Juvenelle thought that clinically the risks of hypothermia should be balanced against the surgical risks He commented on the poor elimination of barbiturates from the body in the cold state

APPLICATION OF THE HEART-LUNG MACHINE TO MAN

Dr D G MELROSE recalled that, while hypothermia is a means of reducing the oxygen needs of the body, the artificial circulation is expressly designed to add oxygen He briefly described the principles of the machine he has designed and showed how a similar machine has been used to aid a patient with very severe pulmonary fibrosis The apparatus is not yet sufficiently developed to take over the whole circulation but can be used safely for a part Deep hypothermia to levels below 26°C is unsafe, yet to obtain a reasonable time—say an hour—in which to operate within the heart by this method, a temperature of about 10°–7°C would be needed In Dr Melrose's opinion, it is best to reduce the temperature of the body to a safe level, and one at which the heart lung machine can adequately take over the circulation when the heart is stopped This, he thought, is how hypothermia and the heart lung machine are likely to be combined in the future He has been impressed with the difficulty of reversing ventricular fibrillation in the cold state, and prefers to avoid this complication

DISCUSSION

Dr C F SCURR described three cases in which hypothermia had been used successfully for cardiac operations in children He noted that the temperature fall might overshoot the desired level despite the start of re warming In these cases, though bradycardia was pronounced, no signs of increase in cardiac irritability were noticed despite direct handling of the heart

Dr CECIL GRAY has had experience of hypothermia in 30 cases He remarked on the value of the lytic cocktail for preventing shivering, and regarded chlorpromazine as the active ingredient from this point of view In adults this is in every respect a preferable method of preventing shivering to either anæsthesia or curarisation. He drew attention to the overshoot in temperature fall which is likely to occur following the opening of the thoracic cavity It appears that at temperatures below 26°C manipulation of the heart may precipitate fibrillation, a further danger at the low temperature is that there is interference with blood clotting—a particularly dangerous effect where there is liver damage with lowered prothrombin Dr Gray suggested that at our present state of knowledge the advantages do not outweigh the dangers of temperatures below 28°C

Dr J W DUNDEE said that the decrease in oxygen consumption produced in animals by chlorpromazine seemed to be greater than that produced by morphine He had used the drug in combination with mild hypothermia for some cases of thyrotoxicosis, and in these cases he had brought the pulse-rate to normal levels before operation, when more usual medical methods had failed.

Most other speakers were impressed with the value of both the anti histamines and artificial hibernation in anæsthesia and in other branches of medicine, but some asked whether a large number of the cases suggested as suitable could not be anæsthetised with equal success by more orthodox techniques

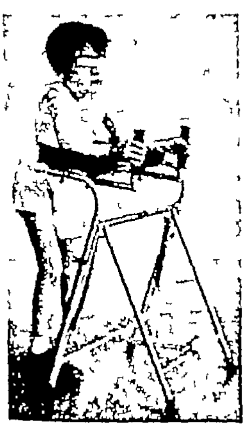
New Inventions

SPRING-ASSISTED WALKING AID

NUMEROUS devices have been constructed for the use of patients who have difficulty in keeping their balance or are apprehensive about the use of crutches during rehabilitation following lower-limb fractures. The apparatus described here gives patients a feeling of confidence because it is exceedingly stable and, being spring assisted, calls for very little effort during movement.

It is made from tubular steel in the form of two pairs of legs, front and rear, held rigidly apart by welded steel tubes parallel to the ground and articulating at the apex by a similar length of tube. Two lengths of steel tube are welded to the outer sides of the rear legs. Into these fits a framework carrying upholstered arm rests and rubber-covered hand-grips. Simple clamping devices are provided to allow for variations in both height and width of the combined hand-grips and arm rests.

A sliding frame mounted on the lower cross members of the front and rear legs incorporates an adjustment for the length of stride and a swivel device to permit folding of the apparatus for storage or transport. A pair of springs between the front and rear legs give sufficient tension to open the apparatus to the fullest extent of its "stride."



With the patient standing upright close to the rear legs of the apparatus, the framework for the arm rests is adjusted so that the patient's forearms, when flexed to a right angle, rest comfortably on the arm rests.

The length of stride may be altered by the adjustable stop on the sliding framework between the front and rear legs.

With the legs of the apparatus in their fully extended position the patient is instructed to lean slightly forward pushing against the hand-grips. This causes the rear legs to leave the ground as the patient's weight falls on the front legs. The patient next leans on the forearm rests, causing the rear legs to swing forward into the closed position when, on continued forearm pressure they will come to rest on the ground. At this point the patient should take a step forward. When the patient removes the weight from the forearm rest and gives the hand grips a slight upward tilt, the front legs leave the ground, and their controlling springs cause them to extend fully. The cycle of movement is then repeated.

The apparatus has been made in two sizes to suit adults or children, and incorporates simple adjustment for height, width, and length of stride. Since the legs fold together, it is convenient for transport or storage.

It has been found useful in the rehabilitation of a wide variety of locomotor disabilities—e.g. cerebral palsy poliomyelitis, disseminated sclerosis, and other neurological conditions with a disturbed sense of balance. In the rehabilitation of the aged and in orthopædic cases it gives patients a much greater feeling of confidence than do the traditional types of walking-aids. Since the apparatus is spring assisted very little effort is required in its use. This feature is particularly striking in poliomyelitis patients with a greatly weakened hand grip who find the manipulation of crutches so difficult.

The Swindon Hospital Management Committee have made funds available for the development of this apparatus. It has been made by the firm of Spenser Harris, Engineers, Cirencester to whom I am indebted for much help in its development and construction.

Liddington Wilts

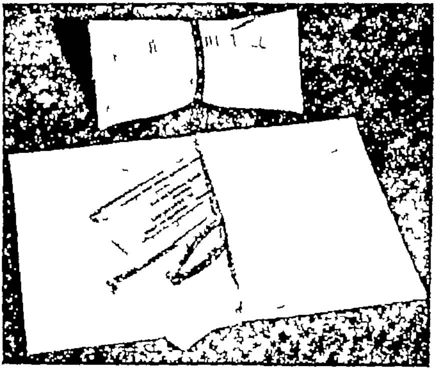
J B STEWART
M.B Edin , D.PHYS.MED

PLASTIC SPECIMEN-POUCH

THE transfer of large specimens from the operating theatre or the post-mortem room to the histology department poses a recurring problem to theatre sisters and pathologists, particularly in areas where the laboratory serves outlying hospitals. Many specimens—e.g., mastectomy specimens—are too bulky for the largest size of screw-capped jar, and it is customary to send such specimens in dressing bowls, hand bowls, kidney dishes, all-glass jars, &c., which are heavy and cumbersome, often leak in transit and must be returned later to their owners. Sometimes large specimens are forced into glass containers of inadequate capacity and their removal after fixation may necessitate cutting the specimen in the jar or even breaking the jar. Moreover the lack of suitable containers encourages the undesirable practice of sending to the laboratory small representative pieces instead of the whole specimen.

The pouch described here was designed to overcome this difficulty. It has proved a satisfactory alternative to metal and glass containers and is preferred by those who send and those who receive specimens. The design and method given below may be modified to suit individual tastes and requirements.

The pouches are made of white opaque Denlon plastic, and are issued to theatres in batches of two sizes.



The smaller pouch with the flap extended measures 16 × 10 in. and the larger 18 × 12 in. Each pouch contains a piece of folded lint 15 or 18 in. square a broad rubber band and a request form. The histology department of the hospital is printed free-hand with a ball point pen on the outer side of the flap; the printing withstands washing and rubbing, and is intended not only to indicate the destination of the specimen but also to prevent misappropriation of the pouches.

Theatre sisters are given the following instructions:

(1) Soak the lint square in 5% formol-saline and squeeze out excess of fluid. Wrap the specimen in the moistened lint (fluff side next to specimen) and place it in the pouch.

(2) Complete the request form and place it between the pouch and the flap. Close (with a fold if necessary) and secure with the rubber band.

(3) Do not delay sending the specimen to the laboratory the formol-saline acts as a preservative rather than a fixative.

When the specimen reaches the laboratory it is removed from the plastic pouch and transferred to a vessel containing fixative until ready for examination. If a tank is used *for fixation and storage the lint can be noosed with* string to form a bag for the specimen.

After use the pouch is washed, dried, and prepared for reissue. The plastic is inexpensive, tough and durable and can be used repeatedly.

These pouches can be obtained from Charles Thackray Ltd. Leeds.

Kent and Canterbury Hospital,
Canterbury

G. B. FORBES
M.D Aberd

Reviews of Books

Our National Ill Health Service

Surgeon Vice-Admiral Sir SHELDON F DUDLEY, K C B, M D, LL.D, F.R C P, F R S, medical director general, Royal Navy, June, 1941-January, 1946 London Watts 1953 Pp 225 15s

THIS is a stimulating and provocative book in which every reader, no matter what his views, will find something to applaud and something to deprecate, probably with equal enthusiasm Sir Sheldon Dudley's main thesis is that the National Health Service is misnamed, since 90 % of its effort and finance is put into curing or caring for the sick and only 10 % into preventing disease, that this disproportion needs correcting, and that the Services have a great deal to teach the civilians on this matter In the process, like a lively dog that cannot pass a side-path, he rushes down some fascinating byways, ranging from placebos to chimneysweep children, and from " the atebrin story " to speculations on the effect of successful psychiatric treatment on Dr Johnson, Darwin, and Florence Nightingale His main sections are entitled the preservation of national health, debunking, the preservation of global health, the Army's struggle for hygiene discipline (an example for all health administrators), and the preservation of health in the Royal Navy (a guide to all defenders of national health) His arrows hit so many targets—some, indeed, shooting down his own arguments—that we stand delighted and forget to take cover until a shaft whistles in our own direction There are occasional slips *our* Sir John Simon was never made a peer, however much he may have deserved it, and Prof James Mackintosh was one time C.M.O of the Department of Health for Scotland, not of the Ministry of Health In his unfavourable comparisons of the civilian health services with those of the Army and Navy, Sir Sheldon acknowledges the advantages of discipline and the ability to give orders but perhaps fails to give due weight to the selected character of the Service " herds " The particular preventive programmes on which he would concentrate if his opinions prevailed, and finance were no object, are not entirely satisfying—being limited to health centres (including the Peckham experiment), research into the social sciences, and the abolition of pneumoconiosis. But his book deserves to be widely read, as the product of real professional eminence a warm heart, an informed mind, and a point of view which has been too much neglected in our National Health Service

Parkinson's Disease and its Surgical Treatment

LESLIE C OLIVER, F R C S, neurosurgeon, West End Hospital for Nervous Diseases London H K. Lewis 1953 Pp 88 12s 6d

IN this monograph Mr Oliver presents his results of spinal cord surgery for the relief of parkinsonism At first he used the original Putnam procedure of lateral pyramidotomy, and he concludes that this operation is rarely indicated for bilateral tremor, but that it brings improvement in about half of unilateral cases More recently he has extended this operation to complete the section of the lateral column

In 14 such cases the tremor was substantially relieved for at least a year to the time of follow up, but at the cost of a permanent contralateral analgesia and of homolateral hemiparesis sometimes quite mild The postoperative Horner's syndrome usually cleared up Nevertheless, these results show that the unilateral tremor must be long standing and the disability severe to justify the procedure, and Mr Oliver believes that its use in a steadily progressive case can only make matters worse

This work affords further evidence that the pyramidal tract in the cord is not the discrete bundle of the anatomical textbooks The variability in the hemiplegia following its section, and the fact that, broadly speaking, the more extensive the lateral section the better the chance of relieving tremor and the greater the risk of hemiplegia, suggest that, though the fibres of the lateral pyramid [illegible] t are concentrated in the posterior half of the lateral column, they are distributed throughout this column Thus the difficulty of forecasting the effect of operation in an individual case is understandable.

The possibilities of cerebral surgery in this condition are also considered briefly The place of surgery here is still undecided, and Mr Oliver concludes justifiably that "there is at present no cure for Parkinson's disease, but in a small proportion of cases substantial improvement may be accomplished by surgery if great care is taken in the selection of patients "

Rudolf Virchow

ERWIN H. ACKERKNECHT, chairman, department of history of medicine, University of Wisconsin. Madison University of Wisconsin Press. 1953 Pp 242 $5 00

WE are apt to think of Virchow as a pathologist only, albeit the greatest of modern times Dr Ackerknecht shows us, however, that he was a gifted and many sided man who would certainly be remembered for reasons other than his contributions to pathology

From his youth onwards he was a social reformer, and he was conspicuous on the barricades in the revolution of 1848, the goal of which was to him the liberation of the working man In the city council of Berlin, to which he was elected in 1859, and in the Prussian parliament, where he remained from 1861 until his death in 1902, at the age of 81, he championed the cause of social reform and on one occasion he was challenged by his opponent Bismarck to a duel As an anthropologist he shattered the myth of Teutonic superiority and made important investigations on Trojan, Egyptian, and Etruscan cultures. In medicine his influence was felt far outside the circles of academic pathology When he went to Berlin in 1856 he asked for, and for many years directed, a clinical division of the hospital, and with the aid of Frederick III he established the first children's hospital in the Prussian capital Public health, sanitation, school reform, and reform of the medical profession all interested him. In addition he was a medical historian.

Dr Ackerknecht, in his scholarly book, attempts to review the work of Virchow and assess his influence during the second half of the 19th century in the fields of medicine, anthropology, and German liberalism, and gives a masterly account of the development of the science of pathology of that time, and especially the history of the cellular theory As a biographer he is accurate and strictly fair in his appraisal of a figure who was in danger, until this volume appeared, of becoming legendary His admiration for him is clearly profound " His greatness," he writes, " transcends the fields he worked in or the nation he belonged to " Dr Ackerknecht is well qualified to write on Virchow because not only is he a doctor, anthropologist, and medical historian, but being a native of Virchow's home province he knew many of his acquaintances.

Handbook of Practical Bacteriology (9th ed E & S Livingstone 1953 Pp 677 25s) —' Mackie and McCartney " has no rivals, and there must be very few bacteriological laboratories that are without a well thumbed and battered copy—which can now go into honourable retirement The latest edition shows no major changes but many new methods have been introduced, and material that was formerly collected in appendices now finds a place in the text These changes have produced only a small increase in the size of the book The technical section is particularly valuable for its excellent articles on microscopy and media-making and there is a new section dealing with the filter paper disc method of testing sensitivity to antibiotics. Inevitably, some bacteriologists may miss one or other of their favourite methods or media for instance, in describing Jungmann's method for the liquefaction of tuberculous sputum, 1 vol hydrogen peroxide is recommended though 10 vol is almost certainly better The section on virus diseases might usefully include information on the types of specimen that are required by the laboratory for diagnostic purposes, and a table of instructions about the time and method of collection and dispatch would be helpful and could perhaps replace the present lists of human and animal diseases due to viruses There is no doubt that the book will maintain its reputation as a thoroughly reliable, practical, and amazingly comprehensive guide to bacteriological technique

THE LANCET

LONDON SATURDAY, DEC 19, 1953

Infection at Work

In any occupation which involves close contact with the public and the public's germs, there must be an increased risk of infection. Less obvious, however are risks which may follow changes in the organisation of man power in industry Since the beginning of the Industrial Revolution in this country around 1820, the movements and aggregation of people at work in factories have had serious epidemiological consequences Susceptible people from the country became crowded together both in their new homes and at their place of work in the towns, and, despite the raising of the standard of living by increased productivity the toll of infectious disease in general, and of tuberculosis in particular, increased ominously Even now, the evolution of our industrial society is not complete, and against the production engineer's cry for bigger and apparently better workshops, Dr ALICE STEWART and her colleagues at Oxford have sounded a persistent note of caution. They have been mainly concerned with the prevalence of tuberculosis in the boot and shoe factories centred around Northampton The alarming rise in the tuberculosis death rate in that industry dates from the move, towards the end of the last century, from cottage workshop to modern factory—a move which increased the size of the working group CAIRNS and STEWART[1] believe that in the rise and fall of tuberculosis mortality over the last century in, for example the printing trade we are seeing a slow motion epidemic starting with the exposure of large numbers of susceptible people to infective carriers in crowded factories, and dying away as all epidemics must when there are no more susceptibles in these industrial communities The unusually high mortality rate from tuberculosis in trades such as printing can be partly explained by the attraction which this work has for men of less robust physique who may choose such an occupation early in life or turn to it later because they cannot cope with heavier jobs. But a study of the results of medical board examinations of recruits coming from the boot and shoe trades does not suggest that this is an important part of the explanation In industrial communities such as those in Northampton there is much contact in the home as well as in the workshop and there is some evidence of the house-to-house spread of tuberculosis in this city,[2] as in others[3] More important, however seem to be wide differences in the incidence of tuberculosis among men working in different factory environments An analysis[4] of surveys by mass miniature radiography in the boot and shoe industry and of notifications of pulmonary tuberculosis showed that among factory workers the incidence of tuberculosis was more closely related to the size of the working group than to the ventilation or other physical characteristics of the factory HEWITT and STEWART[5] showed that although there is an apparent connection between the incidence of tuberculosis in a factory unit and the area of work space per worker in it the association is more apparent than real, since the less crowded workshops tend to house those with heavier jobs—with appropriate names like "rough stuff"—so that the less robust workers may seldom find employment there Indeed, within occupational groups, the tuberculosis notification rates are found to be highest, not in the smaller "overcrowded" work spaces, but in large production units—often well lit and well ventilated—where many workers are in continual daily contact Where these larger spaces are divided by partitions there is evidence that tuberculosis morbidity is less.

In attempting to express these relationships in quantitative terms, HEWITT and STEWART first show that there is no simple constant ratio between increases in the number of workers in the occupational unit and the incidence of tuberculosis among them—in other words, the graph relating the one to the other is not a straight line The curve could be better expressed mathematically by introducing higher powers of the number of people in the unit, but such a curve, unlike the graph of the actual observations, would not tend towards a fixed maximum. HEWITT and STEWART therefore prefer to restate an epidemic theory used by FROST[6] this expresses the incidence of a disease within a closed community, such as a workshop, as the product of the number or proportion of susceptibles and the risk of their making effective contact with an infected member of the group On this basis the risk of becoming infected by effective contact with a carrier can be worked out for groups of various sizes In this instance, neither the proportion of susceptibles nor the carrier rate was known, but they were estimated from the data, and these estimates were used to give theoretical expressions which describe very precisely the way in which the risk of infection varies between working groups of different sizes What is more estimates can be made of the proportion of cases of tuberculosis among adult workers which may be attributable to contacts not made at work. This proportion depends on the size of the working group and ranges from 40 to 60% and it may also be affected by the total population of the factory enclosing these individual work spaces or groups.

The same theory has been applied in a further study of the spread of infection among office staffs. During the 1951 influenza epidemic, ACHESON and HEWITT[7] traced the spread of influenza among the employees of the University Press at Oxford They found it impossible to relate the incidence of the disease either to the closeness of people to one another or to the crowding of the office, as measured by the average area per worker But there was some indication that the attack rate was lower in the rooms with fewer people in them With a disease like influenza where the carrier rate is perhaps as high as 5% and where each infected person becomes an added source of infection, the same theory is not entirely appropriate But it can be used to point out the likelihood that, since the probability of escaping infection depends upon the level of the carrier-rate, a high initial carrier rate, as in influenza, means a rapid saturation of a highly susceptible group with infection. In these circumstances, any increase in the size of the working group beyond a certain point, say 20 workers, makes little difference to the group's attack-rate during the epidemic It is thus hardly surprising that among the workers in the large rooms of the Post Office building surveyed in the epidemiological inquiry described in this issue by Dr **Reid** and his colleagues, there is no striking difference between the attack-rates for the common cold in different rooms

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[1] Cairns M., Stewart, A. *Brit. J soc Med.* 1951 5 73

[2] Webb J W, Stewart A., Sutherland I *Ibid* p 13.

[3] Deeny J *J med. Ass. Éire,* 1947 21 82

[4] Stewart, A., Hughes, J P W *Brit med. J* 1948 i 926

[5] Hewitt D Stewart, A *Brit. J soc. Med* 1951 6, 209

[6] See Zinsser H. Wilson E. B. *J prev Med., Baltimore* 1932 6, 332.

[7] Acheson, F Hewitt, D *Brit J soc Med* 1952 6 68

It would be easy for an armchair critic to suggest reasons why the dangers of cross-infection at work are more apparent than real Differences in office size, for example, may be associated with considerable differences in sex and age composition, in jobs, and in social position—all of which are certainly relevant to the incidence of infectious disease By reason of their size, large offices tend to have poorer industrial morale and lower standards of reporting the true causes of absence In chronic infectious illness, such as tuberculosis, large offices with a high rate of labour turnover make any estimate of the real numbers of effective human contacts over a period of work rather vague That 40% of tuberculous infections among adults are due to work contacts is at best, therefore, an informed guess , but that the risks are appreciable is seen in the doubling of the infection-rate among urban children after leaving school [8]

Some of the practical difficulties of these investigations can be overcome, as in the Post Office study, by systematic interviewing and by combining morbidity surveys with objective measurement of environmental conditions and bacterial contamination of the air The effect of climate may seem to have been all-important , but, of the colds where a history of known contact could be obtained, nearly half were presumably contracted at work A third of the sickness absences in industry are due to respiratory disease , so there is good cause to pursue these preliminary essays in epidemiological method

Radiotherapy and Bronchial Carcinoma

It is hard to find out how far radiotherapy prolongs the life of patients with bronchial carcinoma In general, those selected for treatment of the primary tumour are in a less advanced stage of the disease than those rejected , and to compare the subsequent history of the groups is not a valid measure of the effect of treatment Even if the groups are assumed to be comparable, the effect on survival-time is apparently not very great Thus, in the Survey of Cancer in London,[9] the mean duration of life of untreated patients was found to be nine months , among the treated patients, the expectation was sixteen months for those without evidence of metastases and thirteen months for the larger group with metastases Although there are many reports about the survival of patients after radiotherapy, few include details of the palliation achieved **Brown** [10] recorded the results in 189 patients treated at St Bartholomew's Hospital , in 53% the symptoms were improved, in 21% they were unchanged, and in 26% the condition after treatment was worse than before And the improvement was short-lived in many of those who benefited Only about a quarter of those treated were better for longer than three months, and only 20% survived longer than a year

Palliation is the mitigation of suffering , and suffering is very difficult, if not impossible, to measure Symptoms and suffering are not the same, for a patient may lose his pain but suffer much more from the frequent journeys to the hospital, the loss of work and money, and the knowledge that X-ray treatment usually means cancer On the other hand, his cough and dyspnœa may be worse, but he may suffer less because something dramatic is being done to help him The assessment of change under such circumstances is bound to be much influenced by the enthusiasm of the observer Certain types of suffering, however, can be more accurately described and recorded than others Compression of the superior vena cava, for instance, can cause such distress and such gross physical signs, that the effects of radiotherapy can be measured with little subjective error Yet it is difficult to find facts about it **Brown**,[10] for example, found that the condition was relieved in 18 out of 39 patients, but he does not state in how many the symptoms returned before the patient died and whether, when they did, they were as distressing as before treatment Changes in the distress caused by rapidly accumulating pleural effusions can be more precisely assessed , for the frequency of aspirations required to keep the patient comfortable before and after treatment can be compared There have been several reports of the use of intrapleural radioactive isotopes for this purpose [11-15] **Seaman** et al [15] have treated 40 patients, who had effusions due to primary or secondary intrathoracic neoplasms, with radioactive colloidal gold (Au^{198}) 11 patients died within a month and contact was lost with 3 others But in 20 of the remaining 26 the formation of fluid appeared to have been inhibited, and 9 survived longer than six months The procedure seems simple to carry out and causes the patient little discomfort, though some patients had nausea and vomiting and felt tired for a day or two after the injection Blood stained effusions may become clearer and malignant cells may disappear from the fluid [14] **Walton** [13] treated 18 patients in this way and he considered that 7 had benefited greatly and 4 slightly He noted that those in poor general condition appeared to deteriorate more rapidly after treatment, and it seems reasonable to treat such patients only if the symptoms due to the large effusion are very distressing indeed The diminished formation of fluid may not become apparent until a few weeks after treatment

Radioactive isotopes have also been used to attack the primary tumour in the lung **Muller** and

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[8] Medical Research Council National Tuberculin Survey *Lancet* 1[illegible] [illegible]775

[9] H[illegible] L. Survey of Cancer in London. British Empire [illegible] paign 1952

[10] Brown D E M. *Brit J Radiol* 1952 **25**, 472

[11] Kent, E M. Moses C *J thorac Surg* 1951, **22** 503

[12] King, E R. Spicer D W , Dowda, F W Bender M. E., Noel, W L *Amer J Roentgenol.* 1952 68 413

[13] Walton R. J *J Fac. Radiol. Lond.* 1952, 4, 130

[14] Andrews G A Root, S W , Kerman, H. D , Bigelow, R R. *Ann Surg* 1953 **137**, 375

[15] Seaman, W B Sherman, A L, Bonebrake, M. *J Amer med. Ass* 1953, **153** 630

ROSSIER [16] injected radioactive gold into a branch of the pulmonary artery of animals by means of a cardiac catheter, and they have done the same thing in 4 patients The gold was carried on particles of charcoal of such a size that they were arrested in the fine blood vessels of the selected lobe BRYANT et al [17] used the intrabronchial route in dogs instilling the colloidal gold solution into a segmental bronchus or injecting it in the wall of the main bronchus There was considerable necrosis of the selected part of the lung but high radioactivity was demonstrated in the draining lymph nodes HAHN and CAROTHERS [18] found that silver-coated gold colloids spread more rapidly in the lymphatics of dogs and caused less lung damage Even so, much necrosis followed. There was considerable variation between different dogs in spread and concentration of the isotope in the lymphatic system The presence of a lung tumour and malignant tissue in the lymphatics might make the spread in man even more variable than in animals HAHN et al [19] used the silver coated gold in a patient with advanced bronchial carcinoma, a total of 78 millicuries being introduced into the bronchi of the affected lung on three occasions within ten days The patient tolerated the gold well and high radioactivity was demonstrated in the mediastinal region, but he died fifty days later There were no gross lesions in the lung that could be attributed to irradiation necrosis, although microscopically there was considerable inflammatory reaction. HAHN et al. suggest that the method may be useful preoperatively, the isotopes being introduced into the mediastinal lymphatics by way of the non affected lobe of the lung about two weeks before pneumonectomy, as the lung would later be removed some necrosis of healthy tissue would not matter But it is frequently impossible to be certain before operation that the lung can be removed Nevertheless the method offers some prospect of attacking metastases in the mediastinal nodes Radioactive cobalt has also been used to irradiate the hilar region after lung resection, the cobalt solution was introduced through a catheter into a bag which was kept in a position overlying the hilum and removed after a week.[20] The catheter was passed through a stab incision in the chest wall after pneumonectomy This procedure seems potentially unsafe, for it irradiates not only any tumour left behind but also the bronchial stump and the divided vessels, and high voltage irradiation of the hilar region, either before or after resection, is suspected to have caused bronchial fistulæ and empyemata

It is clearly necessary to explore every means of treating patients with bronchial carcinomas Since the great majority cannot be treated surgically, either because the disease is too widespread, or their general condition too poor, any new method of palliative treatment is worth investigating There may be in hospitals a tendency to divide patients into "treatable" and 'untreatable' groups and if the surgeon cannot remove the lung, to return the patient to the care of his general practitioner with the vague recommendation of symptomatic treatment MAYER and ROSWIT [21] have assembled an impressive list of what can be done to prolong useful life and ease the manner of dying, the methods they mention range from the 23-million volt betatron to high protein diets with emulsified fat supplements, from posterior rhizotomy to preprandial brandy and narcotics On the other hand, it is certainly possible to add to the patient's suffering in the attempt to ease it, and radiotherapy sometimes achieves less than drugs wisely used by a skilful general practitioner

Non-gonococcal Urethritis

ACCORDING to the report of the chief medical officer of the Ministry of Health, in 1952 new cases of non gonococcal urethritis in men attending public venereal disease clinics numbered 11 552, and new cases of gonorrhœa in men numbered 15,510 Non gonococcal urethritis has become an important problem for venereologists not only in this country but throughout the world, for gonorrhœa can now be quickly and easily treated by chemotherapy but non gonococcal urethritis is much less amenable to treatment.

Penicillin is ineffective against non gonococcal urethritis. Good results have been claimed for sulphadiazine [22] but not all venereologists agree on the efficacy of this drug given alone In any event the effect of treatment is not easily assessed, because the course and severity of the disease vary Furthermore, relapses are not uncommon, and observers may differ according to whether they ascribe recurrence of a discharge to relapse or to reinfection. HARKNESS [23] has now reported on 760 cases of the disease treated with the newer antibiotics, in an additional series of 156 patients the drug was chosen by random selection Success was greatest with oxytetracycline (terramycin) in doses of 0·5 g 6 hourly for 4 days, this gave 87% of cures Aureomycin was successful in 63% of cases, while streptomycin and chloramphenicol were less successful with 39% and 36% of successes. LYALL [24] has sought a method of treating both gonococcal and non gonococcal urethritis without masking the signs of syphilis acquired at the same time Such a method could be used in merchant ships which have no doctor LYALL found that one deep injection of 1 g of streptomycin, combined with 30 g of sulphathiazole in divided doses over 5 days, was effective in 93% of 182 cases of gonorrhœa and in 85% of 110 cases of non gonococcal urethritis These very encouraging results suggest that the newer antibiotics—particularly aureomycin and oxytetracycline—should be given routinely in the treatment of non gonococcal urethritis. Further experience will show whether they diminish the risk of complications and relapse.

HARKNESS drew attention to a close correlation between the bacteriostatic action of the antibiotics on pleuropneumonia like organisms isolated from urethral discharge and their clinical effect in non gonococcal urethritis The pleuropneumonia group of organisms are not well known to many medical bacteriologists although several species of the group—including the type species, the organism of contagious bovine pleuropneumonia—are of great importance as pathogens in veterinary practice **Edward** [25] examined the possibility that organisms of this group caused non-gonococcal urethritis, but was unable to decide from the existing evidence whether they were pathogenic in the genital tract of man and animals Since then he and **Nicol** [26] have isolated such organisms from the urethra of 26% of 140 men with non gonococcal urethritis This proportion of positive isolations is similar to that reported by other workers, so apparently three-quarters of cases of non-gonococcal urethritis may be unassociated with pleuropneumonia-like organisms There was no difference in the course of the disease, the response to treatment, or the liability to complications between patients with positive cultures and those with negative cultures In a control group of 90 men with no evidence of genital infection, positive urethral cultures were obtained from 11%, including 3 isolations from men who denied sexual intercourse **Nicol** and **Edward** also showed that there was no serological or other difference between strains isolated from cases of urethritis and strains isolated from healthy men. These workers regard the pleuropneumonia-like organisms as commensals of the human genital and lower alimentary tracts which play no significant part in non-gonococcal urethritis It is, however, possible that these genital strains, and other strains which inhabit the mouth, may occasionally produce localised suppurative lesions or blood-stream infection, and pleuropneumonia like organisms have been isolated from a few cases of brain abscess [27 28] and Henoch's purpura [28] Therefore, although there would seem to be little advantage to be gained from seeking these organisms routinely in cultures from genital infections, the possibility of their presence in suppurative and septicæmic conditions of unknown origin should be borne in mind

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[16] Muller, J H., Rossier P H. *Acta radiol., Stockh* 1951, 35, 449.
[17] Bryant J R., Berg H F Christopherson, W H *J thorac. Surg* 1953 26, [illegible].
[18] Hahn, P F., Carothers, E L *Ibid* 1953, 25 [illegible]
[19] Hahn, P F Hilliard, G. W., Carothers, E L. *Brit J Radiol.* 1953 26 [illegible]
[20] Schneidrzik, W E. J *J thorac. Surg* 1953 25 337
[21] Mayer E., Roswit, B. *Dis. Chest* 1952 21 491
[22] Babione R. W Graham, R. S. *Amer J Syph* 1952 36 480
[23] Harkness A. H *Brit J vener Dis* 1953 29 134
[24] Lyall, T *Ibid*, p 151

Non-gonococcal urethritis has been ascribed also to a virus, but for this there is still very little direct evidence Intracellular inclusions, some of them suggesting the presence of a virus, have been described, but other observers have failed to confirm the presence of these inclusions in a significant proportion of cases The cause of the disease is thus still a mystery, and there is a strong case "for an organized investigation into this condition, with adequate financial support, in which bacteriologists and clinicians should combine their resources" [29]

Metastatic complications, including arthritis, are not uncommon in non-gonococcal urethritis **Ford** [30] has reinforced **Harkness**'s view that the arthritis is identical with the arthritis sometimes associated with gonorrhœa (True gonococcal arthritis is very rare, it is suppurative, and gonococci can be found in the pus) This "venereal arthritis" is characterised by self limiting attacks lasting one to twelve months, with a tendency to relapse, the patient may be left with residual deformities of the feet and even ankylosing spondylitis, but rheumatoid arthritis is not a sequel. **Ford** found no evidence that antibiotics affected the course of the disease Corticotrophin or cortisone alleviated symptoms temporarily, but he was not convinced that fever therapy w effective This sombre view of therapy will not b shared by all clinicians **Harkness**,[23] for instanc claimed good results with oxytetracycline or aureomycin, combined with fever therapy Nevertheless many of the claims to have cured arthritis—often associated with eye and skin lesions (Reiter's syndrome)—must be viewed against the natural history of the disease There will be an understandable tendency to ascribe spontaneous remissions to any treatment Particular attention has been paid to pleuropneumonia-like organisms as a possible cause of the arthritis, because several species of this group are known to attack the joints of animals, but isolation of these organisms directly from joint fluids has only twice been reported, and there is at present no convincing evidence that th arthritis is due to such infection

Annotations

TECHNICAL ASSISTANCE

In 1949 the General Assembly of the United Nations made plans for an expanded programme of technical assistance to underdeveloped areas, and a fund was set up which could be drawn on by specialised agencies—the World Health Organisation, the Food and Agriculture Organisation, UNESCO, I L O, and others This fund has enabled these bodies to extend their work far beyond the resources of their regular budgets, and the expanded programme for the first three years has been working a budget of between 20 and 25 million dollars Duri the financial year of 1952, W H O had available, in cas or kind, a little more than 3¾ million dollars under th expanded programme [31], in the same year F A O disbursed 6¼ million dollars. The aid thus given ha been used to send expert consultants to poorly provided countries, to establish fellowships and scholarships, and to set up training and demonstration centres Equipment has not usually been provided, except when it was an indispensable part of other aid Assistance has been given only at the request of governments, and the recipients have had to match the U N aid with substantial sums from their own budgets towards the co of any selected scheme Often the local administrativ costs have been paid by national governments and i some schemes these have been as much as the U N contribution Both W H O and F A.O give figures to show that the aid which they give is no one sided charity, but that, in fact, U N is only helping those who are already genuinely setting about helping themselves Notable schemes financed in part by W H O, with technical assistance, have been the antimalarial work in the Terai region of Uttar Pradesh, in the foothills of the Himalayas, where 100,000 acres of jungle are bein cleared and a 30% increase in production of foods ha already taken place, the campaign to eradicate completely yaws from Thailand and Indonesia, and the setting up, in many parts of the world, of maternity and child-health centres, where local doctors, nurses, and midwives can be trained Since the inception of the programme, F A O have sent 624 expert advisers into the field, of whom nearly half have completed their mission, and 469 fellowships have been awarded to students, mostly from countries with limited facilities for postgraduate work

It is impossible to translate into dollars the value of th knowledge that has been distributed to needy countries in this way Nevertheless, the whole programme of technical assistance is threatening to fall to pieces for want of money Firstly the U N agencies only get their allotments on a yearly basis secondly, contributing countries have reduced their commitments and a 20% cut in all expenditure has had to be made No one who has examined the detailed reports of W.H O and F A.O would dispute that the funds have been well administered and almost all the money profitably invested in schemes likely to advance the health and economic prosperity of mankind. Underdeveloped countries are, after a lag, seeking to make the full possible use of available aid, so that requests for help now exceed resources Both in education and in development long term schemes are likely to do the most good yet, against an uncertain financial background the risk of starting something which may soon be cut off by budget restrictions is a real one. Worries of this kind may lead to the appointment of a specialist for a brief period to give immediate help in a particular plan when it would be wiser to recruit a man prepared for a longer stay and able to give detailed supervision to the whole project

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[25] Edward, D G ff *Ibid* 1952 28 89

[26] Nicol C S Edward D G ff *Ibid* 1953, 29, 111

[27] Paine T F jun Murray R. Perlmutter, I Finland M *Ann. intern Med* 1950 32 554
Carlson H. J Spector S, Douglas H G *Amer J Dis*
ild. 1951, 81 193

torial, *Brit J vener Dis* 1953 29 121

K *Ibid*, p 123

[31] Work of W H O, 1952 Annual Report of the Director General. Geneva 1953 See *Lancet*, 1953 i 980

[32] Activities of F A O under the Expanded Technical Assistance Programme 1952–53 Rome 1953 Pp 88 5s Obtainable from H M Stationery Office P O Box 569, London S.E 1.

There is no solution to these difficulties except a greater degree of financial stability Here the onus lies on public opinion in the contributing countries and it is disturbing to read [33] that the British contribution to this U.N work was cut from 2 1 million dollars in 1951 to 1 3 million dollars in 1952. This seems a trivial economy, and if other countries follow suit, the efforts to help the governments of the backward countries of the world to raise their people above primitive poverty will be seriously prejudiced.

A NEW ANTI-EMETIC

CHLORPROMAZINE hydrochloride (Largactil), a vigorous young near relation of the anti histamine substances, is so far best known in this country for its power to bring about artificial hibernation [34], and this action was discussed at a meeting of the Royal Society of Medicine reported on p 1294 of this issue On the Continent chlorpromazine hydrochloride has also given promising results in the treatment of psychiatric disorders. But its versatility does not end there; for it has a powerful anti-emetic action

Friend and Cummins [35] have treated seventy hospital patients with vomiting from such varied causes as uræmia, carcinomatosis and pregnancy and the effect of drugs such as aureomycin, morphine, and protoveratrine, and the disulfiram alcohol reaction The drug was given intramuscularly or orally in doses of 25–50 mg three or four times a day In almost all cases the vomiting ceased promptly and side-effects were rare, consisting only of mild drowsiness dryness of the mouth, and flushing Yet the other pharmacological effects of this drug suggest that its use as an anti-emetic will not long be untroubled by side-effects It is a ganglion blocking agent with anticholinergic and powerful sympatholytic and spasmolytic actions it acts on the respiratory centre, slowing the rate and augmenting the amplitude of breathing it blocks thermoregulation by a direct action on the hypothalamus, and possibly acts indirectly on the hypophysis, as is indicated by a modification of postoperative eosinopenia and it potentiates the action of many drugs notably the barbiturates, pethidine nitrous oxide, volatile anæsthetics, procaine amide, and curare.

The basis of anti-emetic activity in general has been much clarified by the work of Borison and Wang [36] These workers show that drugs such as apomorphine, to which have been attributed a 'central' stimulant action on the vomiting centre, do not in fact act directly on the centre The emetic response is now known to be carried to the centre in a reflex arc which is initiated at what has been called a 'chemoreceptor trigger zone.' This receptor is situated on the surface of the medulla outside the central nervous system and is activated not only by drugs but also by the vestibular stimuli concerned in the production of motion sickness.[37] The nature of the transmitter is not known, but it is apparently not acetyl choline.[38] If anti emetic drugs act—as conceivably they may—by blocking transmission at this site, it is unlikely that a specific anti-emetic will be found until the transmitter substance is identified Moreover Borison and Wang believe that the central vomiting mechanism cannot be depressed without concurrent depression of closely associated vital functions involved in the emetic syndrome. Borison and Wang give a conservative valediction 'The most intelligent therapeutic approach to clinical vomiting is elimination of the specific cause rather than the general effect'

SPREAD OF PROSTATIC CANCER

IT is well known that cancer of the prostate often metastasises to the bones of the vertebral column but how the tumour emboli get there is something of a mystery The normal channel of venous flow from the prostate is via the inferior vena cava, and it might be expected therefore that secondary growths would first appear in the lungs by arrest of emboli in passage through the pulmonary capillaries. It has been argued that minute emboli might sometimes be filtered through the lungs back into the systemic circulation and so reach the bones Certainly this might happen but a less tortuous route would seem more probable

Franks [38] has reinvestigated this question, taking as his starting point a suggestion by Batson [39] in 1940 that the prostatic veins and the vertebral venous system might be more directly linked. By an opaque injection method Franks has proved that there is a direct link between the prostatic venous plexus and that of the vertebræ and it seems from this work that the distribution of bony metastases in prostatic cancer can most reasonably be explained by the passage of tumour emboli along this channel, which by passes the caval, portal and pulmonary circulations.

Batson originally suggested that obstruction of the inferior vena cava by increased intra-abdominal pressure could predispose to diversion of blood flow from the pelvis into the vertebral venous system The possibility of similar factors in the distribution of venous emboli from prostatic cancer raises interesting practical questions. Coughing straining and increased intra-abdominal pressure from other causes may turn out to be dangerous to the patient with prostatic cancer

PRIMITIVE LEVELS IN SCHIZOPHRENIA

WHEN the nervous system degenerates, the highest levels of function being those acquired latest in the history of evolution perish first. Dr Ada Glynn [40] argues that a parallel process is evident in the decay of the mind in schizophrenia—that as disintegration proceeds primitive mental mechanisms appear and supersede rational thinking It is an engaging theory and she brings forward some well known ethnological findings to support it. Thus it is a common belief, in primitive cultures, that inanimate objects influence people and events. Such objects may be rocks trees weapons, leaves, animals—or words especially numbers and proper names The primitive tribesman, it is said does not distinguish himself sharply from the rest of the universe but believes himself to be constantly influenced by the objects around him and even by objects at a distance Again, primitive peoples often condense their ideas in picture images with more than one component thus a strong man may be represented as a combination of man and an animal (such as a horse) Ritual behaviour of a rhythmic kind is usually practised as a ceremonial. Magical properties are attributed to things, which resemble other things, and to things which have touched one another thus, a piece of coral resembling a bread-fruit is planted under the bread-fruit tree to make it bear better fruit, branches are waved to encourage the wind to blow, the arrow that has pierced an enemy is urned to make the wound inflame Their suggestibility s such that they have only to be convinced that an arrow is poisoned (though in fact it may have nothing deadly on it), or that an enemy has aimed at them with a ghost shot, in order to develop appropriate symptoms These primitive methods of dealing with experience, Dr Glynn thinks, can be recognised in schizophrenics Thus, patients complain of the harmful influence of neighbours and friends, without making any attempt to explain how these external influences act They attach great importance to words, often to neologisms, and seem to attribute magical properties to them, or to repeat them in order to avert disaster Often such neologisms are composite words condensing (like the centaur) more than one idea. Some patients feel compelled to repeat certain words, or think certain thoughts without, having any desire to do so Some refuse to answer to their names and insist on being called by others of their own devising Their stereotyped behaviour has the magical properties of a ritual and recovered patients can often recall the protective intent with which they practised such rituals Their suggesti-lity is indicated, Dr Glynn thinks, by the apparently ysterical symptoms—blackouts, tears, screaming attacks d the like—which are often the first symptoms of their sorder

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[33] Planning 1952, 19 61.
[34] See Lancet, Nov 14 1953 pp 1027 1039 Dundee J W Gray T C, Mesham P R, Scott, W E B. Brit. med. J Dec 5 1953 p. 1237 Dundee J W Scott, W E B, Mesham, P R. Ibid p. 1244 Smith A. Falrer J G Ibid, p. 1247
[35] Friend, D G, Cummins, J F J Amer med. Ass. 1953 153 480
[36] Borison H. L., Wang S. C. Pharmacol. Rev. 1953 5 193.
[37] Wang S C, Chinn, H. I. Fed Proc 1952 11 400
[38] Franks, L. M. J Path. Bact 1953 66, 91
[39] Batson O V Ann. Surg 1940 112, 138.
[40] Acta psychiat., Kbh. 1953 28, 123.

She believes that if these regressions to archaic levels were recognised as such, and kept in mind, the diagnosis of early schizophrenia could be much improved. Three processes are at work mental disintegration, the uncovering of primitive mechanisms at the uncontrolled lower evolutionary levels of the mind, and the interaction between the disintegrated higher and lower levels The mental disintegration is responsible for the slow deterioration of the personality, the loss of interest in personal appearance with apparent apathy and loss of feeling, the loss of ability to concentrate and make decisions, the ambivalence in thought and behaviour, the fragmented conversation, the day dreaming and withdrawal The patient's difficulty in formulating thoughts leads him to pause long before answering a question, and accounts for the worried look so often worn by schizophrenics A common early symptom is unwarranted exaltation, manifesting itself as "a rising conceit with an ever declining performance"—evidence of the vagueness the patient feels about himself and his environment Impulsive behaviour often results from obedience to hallucinations, which are themselves partly the result of projection—one level of the mind accepting as bona fide sensory stimuli the imagery produced and projected by another level But hallucinations are also partly due to suggestibility, which is a characteristic not only of schizophrenic and primitive minds, but also of the mind of the child. Obsessional symptoms resemble schizophrenic symptoms, she holds, in being no longer controlled by those levels of the mind which have evolved later they bear the tamp she says, of magical thinking, and merely epresent another aspect of schizophrenia, even though he symptoms may never progress beyond the obsessional

While Dr Glynn's thesis is suggestive and it is not susceptible of proof at present—and indeed may never be Her confidence in its accuracy goe perhaps a little beyond the bounds appropriate to the detached scientist

NARCOSIS IN THE TREATMENT OF EPILEPSY

DESPITE new remedies for epilepsy, there remains hard core of patients who derive little or only temporar benefit from any anticonvulsant drug or regimen Their plight is sometimes made worse by the fact that their fit progressively narrow the field of work open to them For them, heroic measures seem justified, and they are usually only too willing to try these Putnam and Rothenberg[1] describe a method of "intensive treatment" for these patients it consists basically in narcosis induced with massive doses of hydantoins, supplemented, if necessary, by paraldehyde or phenobarbitone intramuscularly. The patients sleep for four days, and they are then roused by stopping all narcotics and giving amphetamine to shorten the period of awakening Depth of narcosis varies, but in general, continuous supervision and detailed nursing care, already familiar in the prolonged narcosis of psychi-atric treatment, are required Putnam and Rothenberg attach importance to the production of some degree of ketosis and to the intermittent inhalation of carbon dioxide They also give intravenous infusions of glutamic acid. Of 25 patients who had failed to respond to a very thorough trial of other remedies, 16 were rendered seizure-free for follow-up periods of a year or more, and a further 5 were substantially improved. All were maintained in this condition on the drugs, either in the same or smaller doses, which they had been taking without success before the "intensive treatment" These are impressive results considering the unhappy outlook for such patients at present

THE PARIS MEDICAL SCHOOL

ON Dec 3 the President of the Republic opened the new medical school of the University of Paris. It stands at the corner of the Rue Jacob and the Rue des Saints-Pères, on the site of the ancient Charité Hospital where Laennec used the first stethoscope

Building began in 1936 in the crowded area of St Germain des-Prés, and the austere, seven-storeyed school now dwarfs the picturesque and often shabby haunts of famous artists and writers But in Paris the humanities and science still know how to live amicably together, and the massive bronze portal by one of the leading masters may have meaning for some of the 2500 first and second year students who succeed in penetrating a growing doorway scrub of cars and autocycles Eight departments are already at work with the most modern equipment, the physics laboratories are insulated against sound and "les parasites électriques," and there are special facilities for radiology and work with radio isotopes. Lecture theatres have up-to date visual aids and physiology students can peer closely at the most delicate manipulations in the "amphi-théâtre lorgnette." Post-graduates have not been forgotten, and the Société de Biologie, with a long list of famous doctors among its past presidents, hopes soon to meet in the new school.

Dr THOMAS COCHRANE, who died on Dec. 7 at his home in Pinner, Middlesex, at the age of 87, worked a medical missionary in China at the beginning of the century and founded, at Peking, the first medical training college for Chinese students.

AT a meeting of the Royal College of Surgeons of England on Dec 10 it was decided to proceed at once with the building of the Nuffield College of Surgical Sciences.

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[1] Putnam, T J, Rothenberg, S F J. Amer med. Ass. 195 152, 1400

Public Health

COLDS AMONG OFFICE WORKERS

AN EPIDEMIOLOGICAL STUDY

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HE revival of interest in the possibility of preventing common cold and other disorders of the upper piratory tract by the control of airborne transfer of ction has uncovered the large defects in our knowledge he epidemiology of these diseases Before trying to ause trials of control methods we therefore made an demiological study of the incidence of colds and ilar affections among groups of office workers. Our was to relate the incidence of colds to certain ironmental conditions in an attempt to elucidate the de of spread. We here report the results of a pilot vey

With the help of Dr Cecil Roberts, then Deputy asury Medical Adviser we were able to invite the peration of members of the clerical staff of the General t Office working in a block of offices in the City of ndon. Each volunteer gave us detailed histories of or her cold' experience each week during the iod of the survey and at the same time we made ervations on the bacterial content of the office air d on the temperature and humidity in the offices.

Methods

COLLECTION OF DATA

After preliminary discussions with administrative icers and staff representatives a meeting was held to plain to the staff the plan of the survey and to invite ir help Questionaries were issued to each member the staff and were filled in by all those willing to take rt. These were checked for completeness by a nurse vestigator

The volunteers were enrolled in two stages From April, 49, 104 persons in three rooms A, B and C took part the survey In August, 1949 352 volunteers in ten her offices joined. Both groups were observed until pril, 1950 Altogether 92% of the staff volunteered. e intention was to question each person each week, t the second group proved to have a different system working from the first and consequently could only be terrogated once a fortnight. The difficulties of knowing hether a member of this migratory group was sent owing to sickness holiday or other reasons made e information obtained about them so unreliable that e results discussed below come almost entirely from the 4 staff in offices A B and C Of these 104 131 were esent for the whole year of the survey

METHODS OF QUESTIONING

Each week every volunteer in the static group offices A, B and C was questioned by the nurse about s or her experience of colds in the preceding seven days. Those who had had a cold were asked about their symptoms. Chronic coughs were ignored, but for l acute disorders a special questionary was completed giving details of symptoms on the day of onset recognised contacts with other sufferers from colds, possible predisposing experiences and so forth

The definition of a cold' is difficult, and in the present report we have grouped together under this term all minor acute respiratory tract disorders Virus influenza was not epidemic during the winter of our survey, and only about 22% of the incidents recorded were accompanied by symptoms of fever such as shivering The great majority (about 78%) were typical acute rhinitis, and most were accompanied by some soreness of the throat

Since it was clearly futile to try to interpret the frequency of 'contacts among those with colds without some knowledge of the relative frequency of such contacts among those free from symptoms a random sample of the remaining symptom free members of the same office were questioned similarly in the same week So far as possible, the numbers of 'controls' selected for interview were equal to the number with colds

BACTERIOLOGICAL AND ENVIRONMENTAL STUDIES

Visits were made to the offices once a week during the period May–October, 1949 after which it proved impracticable to make visits more frequently than once in two weeks. At each visit air samples were collected in eight to twelve of the rooms selected at random from the twenty four among which the volunteers were distributed, the order of visiting was also random

With a slit-sampler the bacteria-carrying particles from 200 c ft of air were collected on the selected medium of Williams and Hirch (1950) for the detection of *Streptococcus salivarius* and those from 5 c ft were collected on serum agar for a general bacterial count'

At each visit the temperature and relative humidity within the offices were measured. Outside temperature and humidity records were taken from the Registrar General s Weekly Return

Results

During the twelve months of the survey the mean number of colds reported by the 131 persons in rooms A B, and C who were exposed to risk throughout the whole year of the survey was 2 2 The numbers of persons reporting 0 1 2 6 colds in the year were respectively 13 26 40 36 11 3, and 2

We may consider first the factors associated with the individual that may have affected his experience of colds Secondly we may compare the experience of the groups of people in the various offices at different seasons.

PERSONAL FACTORS

The mean numbers of "colds per person among the relatively static population in the three rooms A B and C in each age-group and sex group are given in table I In the total' row and to a lesser extent among females there is a downward trend in incidence with increasing age There were only 12 males aged less than 50, hence it is impossible to judge if the same is true of males. The women had distinctly more colds than the men—

TABLE I—COMMON-COLD EXPERIENCE ACCORDING TO SEX AND AGE

—	Age-group (yr)							
	Under 30		30–49		50 and over		Total	
	No of persons	Colds per year	No of persons	Colds per year	No of persons	Colds per year	No of persons	Colds per year
Males	7	1 7	5	2 6	[illegible]	1 8	51	1 9
Females	36	3 0	22	2 1	[illegible]	2 2	80	2 4
Total	43	[illegible]	[illegible]	2 2	61	1 9	131	2 2

TABLE II—COMMON-COLD EXPERIENCE IN PEAK EPIDEMIC PERIOD 1949

—	Attacked 1–8 weeks previously	Attacked 9–26 weeks previously	Not attacked within preceding 26 weeks	Total
Exposed	48	36	63	147
Attacked in epidemic	17	23	30	70
Attack rate (%)	35	64	47	48

2 4 compared with 1 9—and this difference is not affected by age standardisation

There was also some evidence for short term immunity to the cold As will be shown below, there was a sharp epidemic of colds in the period Oct 29–Nov 19, 1949 Although only 131 people were under observation in the three offices A, B, and C for the whole year, 147 were observed from the beginning of the survey until the end of the epidemic in November, they could be divided according to their "cold" history in the months preceding the outbreak, and the attack-rates in three such categories of them are set out in table II The lowest attack-rate (35%) is among those who had had a "cold" in the eight week period immediately before the outbreak, the highest rate (64%) was among those who had had an attack earlier in the year but not within eight weeks of the outbreak Those with no history of previous attack since April had an attack-rate between these two (48%) The differences are technically significant, and a tentative explanation of them might be that those most susceptible to "colds" are distinguished by their previous history from the relatively immune, who have not been attacked for some time But in the epidemic itself there does appear to have been some short-term immunity conferred by an attack up to eight weeks before

TABLE III—HISTORY OF INFECTIVE CONTACTS GIVEN BY "COLD" SUFFERERS AND BY CONTROLS

History of contact with a "cold" sufferer	Persons with colds (363)		Controls (318)	
At home				
A*	9	56 (15 4%)	4	21 (6 6%)
B*	47		17	
In office				
A	2	45 (12 4%)	1	24 (7 5%)
B	43		23	
Elsewhere				
A	2	17 (4 7%)	2	5 (1 6%)
B	15		3	
None known		245 (67 5%)		268 (84 3%)

A*, contact recognised within last 3 days
B* contact recognised within last 6 days but not specified more precisely

PREDISPOSING CONDITIONS

Short-term immunity may conceivably be affected by predisposing conditions, such as chilling and fatigue An analysis based on the records of all the colds reported in the survey showed that the cold sufferers certainly gave a history of being chilled or fatigued significantly more often than the controls, but there were internal inconsistencies in the data which suggested that no great reliance could be placed on these findings

HISTORY OF CONTACT

Table III is based on all the 363 colds and their available con[illegible]ng both static and migratory groups It shows that a history of contact with other sufferers from a cold was obtained significantly more often from people suffering from colds than from their "controls" In the 32% of cold sufferers who gave a history of a recent contact with an affected individual, almost half named someone at home and half an office colleague These were the main sources of known contacts Even in these instances only 11% of the dates of contact could be placed within the likely incubation period of three days immediately preceding the onset of symptoms, and most cold sufferers could be certain only that contact had taken place sometime within the previous six days. This alone makes the linking of cases rather difficult, and it proved impossible to study the geographical spread within offices, because of the continual changes in siting of desks, jobs, rooms, and contacts

TABLE IV—FREQUENCY OF ATTACK IN DIFFERENT OFFICES

Office	No of persons	No of colds	Attack rate per person
A	44	100	2 3
B	18	40	2 2
C	60	145	2 1
Total	131	285	2 2

COMPARISON OF DIFFERENT TYPES OF CONTACT

Tables IV, V, and VI are based on the experience of the 131 people observed throughout the whole year Table IV shows that, within the range of average number of occupants here observed (18–60), there was no difference in the frequency of colds between people in the three rooms A, B, and C Nor is there in table V any evidence that, in these three offices, colds differed in their clinical patterns No differences could be distinguished in the timing of the epidemic in the three offices

We could not detect any material difference in the numbers of colds suffered by persons living with adults only, compared with those who lived in households containing children Those who lived alone had fewer colds, but their numbers were so small as to deprive these figures of any reliability There were no differences in the cold experience of persons travelling to work by different routes, but there were none who did not use public transport

SECULAR TRENDS IN INCIDENCE OF COLDS

The secular changes in the attack rate for colds in the three offices are shown in fig 1, where the smoothed curve of the number of colds per 100 persons per week shows that there was relatively little change in incidence during the early part of the autumn There was an increase to about 10% in early October, and then, in early November, a very sharp increase to a peak attack rate in one week of 24% The attack-rate fell sharply after this and, although it fluctuated somewhat, there

TABLE V—FREQUENCY OF VARIOUS SYMPTOMS IN 363 COLDS REPORTED FROM THE THREE OFFICES

Symptom	Room A	Room B	Room C
Sore throat	75 (63 0%)	38 (74 5%)	124 (64 3%)
Running nose	104 (87 4%)	44 (86 3%)	168 (87 1%)
Cough	57 (47 9%)	22 (43 1%)	81 (42 0%)
Headache	57 (47 9%)	29 (56 9%)	87 (45 1%)
Fever	26 (21 9%)	12 (23 5%)	39 (20 2%)
Other symptoms	17 (14 3%)	9 (17 7%)	30 (15 5%)
Total no of colds	119	51	193

s no further substantial rise in incidence during the nter

SECULAR TRENDS IN ENVIRONMENTAL FACTORS

The mean bacterial counts recorded in the air in the ces at each of our visits are also given in fig 1 The neral count fluctuated somewhat but showed no nsistent seasonal trend. The *Strep salivarius* count o fluctuated considerably, but there were three periods en it seemed to be consistently high in June and vember 1949 and in March–April, 1950 Owing to rather small numbers of samples examined these nations all need to be interpreted with caution

There was so little variation in the indoor temperature er the greater part of the investigation that the figures e not included in the diagram The outdoor temperature owed no striking autumn fall until mid October ring the last two weeks of October it fell from about °F to about 45°F The outdoor relative humidity o showed a sharp fall at the same time.

ASSOCIATION OF ENVIRONMENTAL FACTORS WITH PREVALENCE OF COLDS

It is immediately clear from fig 1 that the sharp drops outdoor temperature and relative humidity were closely sociated in time with the steep rise in the common-cold tack rate and in the *Strep salivarius* count in the air

BLE VI—" COLD " EXPERIENCE IN CONTRASTED HOME AND TRAVEL GROUPS

Category	No of people	No of colds	Colds per person
micile:			
Living alone	7	13	1·7
Living with adults only	107	235	2·2
" " " and children	17	37	2·3
Total	131	285	2·2
vel to work: Underground	33	83	2·5
" and bus	26	50	2·0
Bus or trolleybus only	13	30	2·3
Main line train only	33	68	2·1
" and bus	11	24	2·2
" " and underground train	16	30	1·9
Total	131	285	2·2

he central heating in the offices was turned on gradually uring the period Oct. 25–28

The sharp increase in colds in early November was not ly simultaneous in the three rooms A B and C, and mong the migratory group in the office, but also general the London area. This was clear in the absence rate r a sample of Post Office workers distributed over the hole area (fig 2) Official notification of pneumonia in he London area followed the same time pattern after a g of about three weeks Fluctuations in the absence ate in the early months of 1950 were not, however, eflected in the common-cold attack rate in our office pulation.

Discussion

The study reported here was made principally to xplore a method of obtaining precise information on the number of colds suffered by a group of office workers so that their incidence could be related to environmental easures, including the bacterial content of the air For disease, such as the common cold, which is of variable verity and often does not lead to absence from work, tatistics of absence may be affected by morale in the

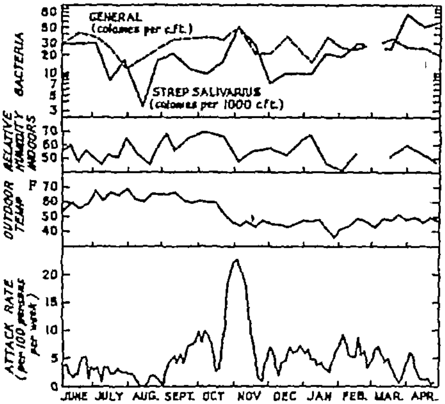

Fig. 1—Environmental factors and incidence of colds.

office, hence the number of absences does not necessarily reflect the number of colds suffered In our experience the number of attacks cannot be satisfactorily discovered by asking the subjects of the investigation to report only when they have a cold nor have we been successful in obtaining the information by circulating brief questionaries. The method now adopted of asking each individual personally each week whether he or she had had a cold in the previous seven days, has two major advantages: not only do we obtain a clear 'yes' or "no" for a period over which memory should be fairly accurate but we also have an opportunity of further questioning those who report a cold. From these supplementary questions one can assess more objectively whether or not the symptoms reported fall into the accepted definition of a "cold"

The success with which an investigation of this sort can be pursued depends very largely on obtaining the confidence of the participants In any large organisation there may be a fear that the results of an inquiry will be used in subsequent considerations of promotion or establishment. This is another reason for appointing a special investigator for the study and not relying on a member of the office staff for the collection of the necessary records.

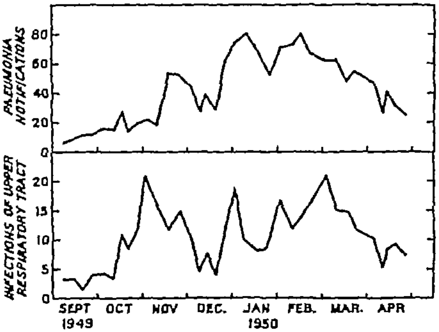

Fig 2—Pneumonia notifications in London and absence-rate per 1000 postmen.

Thanks to the coöperation of the staff in the department studied, we obtained complete detailed records of the experience of colds of 131 persons over one year. Unfortunately the duties of these members of the staff involved them in a considerable amount of movement, both within one room and from one room to another; so it was not possible to trace the spread of colds from one person to his or her neighbours at work.

Persons with colds remembered contact with someone else who had a cold more often than did "controls" who had had no recent cold. This may mean that, in some cases, the recognised contact was the source of the cold, but it may also be that persons with colds are more likely to recall contacts than are those without colds. Further, the fact that our controls were not strictly paired with the cold sufferers for age and sex might account for the difference. Even with these sources of error, only 32% could give a precise account of a contact.

We could detect no great difference in the attack-rate in groups of persons travelling to work by different methods, or coming from households of various sizes and composition. Nor in this urban group could we see the effect of the school child demonstrated in a rural group by Lidwell and Sommerville (1951). There was a suggestion, which in general confirms earlier observations, that the young women had the highest attack rate. There was no evidence that the size of the office populations was related to the risk of having "colds".

There was a suggestive time correlation between the onset of the sharp November outbreak of colds and a fall in both outside temperature and relative humidity; such a correlation was previously demonstrated by van Loghem (1928). During the same week there was a sharp rise in the number of *Strep. salivarius* in the air of the offices—an observation similar to that of Torrey and Lake (1941). A high streptococcal count was observed at two other times, but neither was accompanied by any rise in the incidence of colds in the offices. The association of a high streptococcal count with a high incidence of colds in November might be fortuitous, but if real it could be explained in one of two ways: (1) the onset of cold weather makes people shut the windows; this reduces the ventilation, increases the number of bacteria in the air, and may at the same time facilitate the spread of colds; and (2) alternatively the weather may precipitate the colds, and the sneezing and coughing they cause may lead to the rise in the streptococcal count in the air. Our present data do not allow a judgment between these alternatives, but other studies suggest that the *Strep. salivarius* count responds much less than the general bacterial count to changes in ventilation. The November outbreak was accompanied by little change in the general count; so diminished ventilation alone is unlikely to be the cause of the appreciable rise of the *Strep. salivarius* count.

The general picture of a sharp increase in attack rate over a short period suggests "epidemic" spread through the offices, but the fact that a similar rise in incidence was observed in many other offices in London throws some doubt on this interpretation and suggests that meteorological or similar factors may have been all-important. The elucidation of the part played by case-to-case transfer of infection within the office can only come from more detailed work than was possible in the present study. In particular it will be necessary to observe a group in which any individual's range of contacts is limited and well defined. Some studies of this sort are already in progress.

Summary

Members of the clerical staff of several offices in Central London were questioned weekly during the year April, 1949–March, 1950, about their experience of infections of the upper respiratory tract. 131 persons were observed for the whole year. On the average, each person had 2.2 colds in the year.

The incidence of "colds" appeared to be highest in young women. Although there was evidence of short-term immunity following a cold, no other differences in range of contact at work, in travelling, or at home appeared to affect the attack-rate.

The beginning of a sharp epidemic of colds in November, 1949, coincided with a sudden fall in outside temperature and humidity. At the same time there was a notable rise in the numbers of mouth streptococci in the office air.

Our thanks are due to all the volunteers who took part in this study. We are also indebted to Mr. D. E. Miller for technical assistance. The work was done on behalf of the Air Hygiene Committee of the Medical Research Council.

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The Public's Health in 1952

In two years the death-rates in England and Wales among young women aged 15–25 have fallen by about a third. This striking change is mentioned by Sir John Charles, chief medical officer of the Ministry of Health, in his annual report for 1952.[1]

For this change the reduction in mortality from *tuberculosis* is thought to be largely responsible. In 1952 deaths from all forms of this disease reached a new low level of 10,585, giving a rate of 240 (respiratory 212, non-respiratory 28) per million population. Mortality from this cause has fallen 52% in the last four years. At the start of the year there were 290,389 notified cases of the disease; and by the end of the year the total had increased to 311,702. The number of new cases (all forms) diagnosed during the year was 44,525. About 1 in 7 of these was detected by contact examination.

"It is encouraging," says the report, "to note not only that the number of new cases diagnosed tends to become stable but also that greater and more fruitful use is being made of contact examination. In 1952 more than 8000 more contacts were examined than in 1951 and 4.64 per cent. of them were found to be tuberculous as compared with 3.5 per cent. in 1951."

Deaths from tuberculosis are now definitely exceeded by deaths from *cancer of the lung*, which numbered 11,218.

Two epidemiological features of the year were a further decline in the number of cases of diphtheria and an increase in notifications of scarlet fever. *Diphtheria* accounted for 376 cases with 32 deaths, compared with 664 cases and 33 deaths in 1951. The fatality-rate rose from 5% to 8.5%; in immunised children this rate was 1.1%, whereas in those who had not been immunised it was 9.9%. Cases of *scarlet fever* numbered 67,281 with a fatality-rate of 0.03%, compared with 48,744 and 0.08% in 1951.

Poliomyelitis.—In 1952, 3902 cases were notified, which was substantially below the average for the past five years. The fatality-rate of 7.6% was the lowest since the epidemic of 1947. Non-paralytic cases amounted to 20.8% of the total. Regarding control of spread Sir John Charles writes:

> "Certain simple general principles can enable us to lay down a course of action which is usually effective. Two of the most important of these are the isolation of the patient and the control of those individuals who have been in contact with him during the infective stages of the illness. The degree of isolation to which patients and contacts may have to submit varies a good deal with circumstances. In poliomyelitis the relevant circumstances which have to be taken into account are the ages of the patients and contacts and the amount of infection present in the locality. It has been noted time and again that outbreaks of poliomyelitis tend to occur in small communities such as

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[1] Report of the Ministry of Health for the Year ended Dec. 31, 1952. Part II. On the State of the Public Health, being the annual report of the chief medical officer. Cmd. 9009. H.M. Stationery Office. Pp. 250. 6s. 6d.

HOSPITAL BEDS AVAILABLE FOR ALL PHYSICAL CONDITIONS EXCLUDING PRIVATE PAY BEDS

Specialty	1949 Beds	1950 Beds		1951 Beds		1952 Beds	
		No.	Difference on 1949	No.	Difference on 1950	No.	Difference on 1951
General medicine and surgery	66 071	69 964	+ 3,893	68 135	− 1 829	68 228	+ 93
Gynaecology	7 410	8 217	+ 807	8 745	+ 528	8 878	+ 133
Obstetrics	17 385	18 893	+ 1 508	19,369	+ 476	19 635	+ 266
Tuberculosis	28 307	32 108	+ 3 801	33 774	+ 1 666	34 047	+ 273
Infectious diseases	21,848	20 577	− 1 271	18 143	− 2 434	16,235	− 1 908
Ophthalmology	3 544	3,975	+ 431	4 070	+ 95	4,391	+ 321
Traumatic and orthopaedic surgery	11,816	13 613	+ 1 667	14 301	+ 818	16 721	+ 2 300
Chronic sick	54 387	56 057	+ 1 670	56 930	+ 873	57 705	+ 775
Convalescent and pre-convalescent	6 664	6,779	+ 115	7 124	+ 345	7 150	+ 26
a.r hospitals	7,864	6 499	− 1 365	6 941	+ 442	6 735	− 206
Others	44 642	53 011	+ 8,369	53,883	+ 872	50 640	− 3 243
All physical conditions (excluding private pay beds)	270 058	280 593	+ 10 535	282 475	+ 1,882	281,365	− 1 110

families, nursery schools, school classes or residential hostels. When an outbreak occurs in a day school it is usually the youngest children who are most affected by the virus. It is therefore logical as well as economical in effort to concentrate upon them the preventive measures available The measures most likely to effect control of the outbreak are the two general measures to which reference has already been made isolation of the patients and exclusion of their contacts from school for some three weeks.

Sir John observes that the number of incidents of *food poisoning* suggests that the gospel of kitchen hygiene has scarcely yet affected the practice of food handlers as a whole In 1952 5873 corrected notifications were received by the Registrar General but it is known that more than 11 000 people had symptoms. Altogether 3310 incidents were reported these comprised 372 outbreaks, 310 family outbreaks and 2807 sporadic cases. The presumed causal agents were *salmonella* (2008) staphylococci (82) *Clostridium welchii* (20) other organisms (17); and chemical (1) in 1301 instances the agent was not discovered Between 1949 and 1952 in 55–60% of all outbreaks where the vehicle of infection was established this was processed and made-up meat. In 1952 of all outbreaks (excluding family outbreaks) in which the place where the contaminated food was bought or eaten was recorded, 60 originated in canteens, 28 in restaurants, 19 in institutions, 16 in shops and 6 at private parties.

Venereal Diseases.—Once again at the clinics there was a substantial fall in the number of new patients with syphilitic infections of less than a year's duration: 881 men and 462 women attended for the first time in 1952 compared with 1408 men and 774 women in 1951 The number of cases of congenital syphilis in children under 1 year of age fell to 110 compared with 156 in 1951 Cases of gonorrhœa diagnosed in 1952 numbered 15,510 in men and 3585 in women compared with 14,075 and 3080 in 1951 The significance of this rise is not yet certain, but the possibility of a commencing strain-resistance to penicillin has to be borne in mind" Cases of non gonococcal urethritis in men numbered 11,562, compared with 10,704 in 1951

SOME MORTALITY TRENDS

Diseases of the circulatory system vascular lesions of the central nervous system, and cancer accounted for more than two-thirds of all deaths in 1952 compared with rather less than half twenty years ago. Deaths ascribed to *coronary-artery disease* again increased notably—to 61 420, compared with 40,330 four years earlier

The *stillbirth-rate* (23 7 per 1000 total births) has hardly changed since 1949 and the *neonatal mortality rate* (19 3 per 1000 live births) has likewise changed little since 1950 Sir John remarks

"It is an open question whether we have not progressed as far as our existing knowledge of causes and contributory circumstances can take us and that the way to further improvement lies through research, rather than through the continued exploitation or modification of established methods."

DENTAL TREATMENT

Between 1950 and 1952 the demand for dental treatment on behalf of young people up to 21 years of age rose from 18% to 20% of all applications. There was an almost equal reduction in the proportional demand by patients aged over 45 and the demand by those aged 22–45 remained about the same

UTILISATION OF HOSPITAL BEDS

Among the many other subjects discussed in the report is the utilisation of hospital beds.[2] This section includes a table (reproduced here) showing beds available for all physical conditions, excluding private pay beds, for each year since 1949

THE NEW PUBLIC HEALTH

Sir John Charles urges a fresh outlook on public health

"It has" he says, "been argued with some force that an increased expenditure on Preventive Medicine would *obtain a consequential reduction in the demands on the* treatment services. But to look at the matter realistically surely it would be courting disillusionment and disappointment simply to increase the financial support of the established forms of Public Health activity It is not enough to have more and more of the old remedies for the old ailments of the Public Health. Research in a number of new fields is required—into the causation of the so-called chronic diseases, into the manifold conditions which trouble the mental health of thousands of our fellow citizens, reduce their enjoyment of life and make participation in its tasks and responsibilities a struggle instead of an adventure; into the prevention of the trivial illnesses of everyday existence into the fostering of the physical forces of men and women so that old age comes upon them more gradually and with less sense of restrictive incapacity These are only a few of the comparatively uncharted fields, exploration of which will surely reduce the burden of the curative services.

Industrial Injuries Insurance

Papilloma of the bladder has been added to the list of diseases prescribed under the Industrial Injuries Act. The regulations[3] making this addition came into force on Dec. 7 They provide industrial injuries benefits for persons suffering from the disease as a result of certain specified occupations in which they have been employed at some time since July 5 1948 the date the Act came into operation Most of the occupations covered are in the chemical industry mainly in certain processes involving contact with α naphthylamine β-naphthylamine, or benzidine, or any of their salts. Cover is also given to workers engaged in the *production* of the dyes auramine or magenta there is nothing to indicate that the finished dyes are in any way harmful.

Scotland in the Third Quarter

In Scotland during the September quarter of this year[4] the birth rate of 17 3 per 1000 population was lower than the average for corresponding quarters in recent years, but it was the same as the rates recorded just before the late war The infant-mortality-rate was 28 per 1000 live births, which was 2 less than the corresponding quarter of 1952, 6 below the average for the past five years, and the lowest recorded in Scotland in any quarter The stillbirth-rate was 25 per 1000 total births—an increase of 1 over last year's figure The death-rate of 9 9 per 1000 population was 0 1 less than last year and 0 8 less than the five years' average. The death-rate from all forms of tuberculosis was 21 per 100,000 population (respiratory 18, other forms 3), the corresponding figures last year were 22 (19, 3)

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[2] See *Lancet* Dec. 5 1953 p 1193.

[3] The National Insurance (Industrial Injuries) (Prescribed Diseases) Amendment (no. 2) Regulations 1953. S.I 1953 no. 174 H.M Stationery Office. 3d.

[4] Quarterly Return of the Registrar-General, Scotland Births Deaths and Marriages Registered in the Quarter ended Sept. 30 1953 H.M. Stationery Office. Pp. 30 2s. 6d.

Special Articles

CHOOSING AND CHANGING DOCTORS

P G Gray B Sc Lond.

Ann Cartwright B.Sc Lond.

From the Government Social Survey

The information given here was obtained in the course of an inquiry for the Committee on General Practice of the Central Health Services Council The inquiry was made in conjunction with the Survey of Sickness during February and March, 1952, and is based on 7027 interviews with a randomly selected sample of civilian adults covering England and Wales

Private and N.H S Patients

The people interviewed were asked whether they were on a doctor's list under the National Health Service, and, if so, whether they also received private medical care 97 7%* said they were on a doctor's list, 95 7% relying solely on the N H S, while 2 0% had a private doctor as well The remaining 2 3% were not on a doctor's list

Not all the 2 3% outside the N H S. relied on private practice, for some had not chosen a doctor because they had not been ill According to their replies to the question "what would you do if you were ill," they can be further subdivided The people interviewed then fall into the following five groups

	%
Registered under N H S and not using private practice	95 7
Registered under N H.S but also using private practice	2 0
Using private practice only	1 5
Probably will use N H S when ill	0 6
Probably will use private practice when ill	0 2

Thus in all about 3 7% obtained, or are likely to obtain, medical care outside the N H S

About the same proportion of men and women chose ~~to have a private doctor,~~ and the proportion rose only slightly with age Income was the most important factor influencing the use of private practice The proportion of people not on a doctor's list was small, and showed little change with increase in income, until the head of the household had a weekly income of over £20 a week, when the proportion was ten times the average for all adults

Each informant was asked whether he had consulted a general practitioner during the seven days before the interview, and, if so, whether the consultation was made under the N H S Of the 690 consultations made with general practitioners, 3 2%† were outside the N H S This figure gives some idea of the extent of private practice

Choosing a Doctor

5% of all the adults said that they had a woman doctor, but whereas 2% of men had a woman doctor, 8% of women had one The proportion of women choosing a woman doctor increased slightly with age —from 6% for women aged 21–34 to 10% for those aged 65 and over Thus women doctors tend to have higher proportions of women and old people among th patients than men doctors Both these groups tend make more use of their doctors. Thus, although medical profession is one in which women have pay, they probably do more than equal work for it

77% of men, as against 53% of the women, said th they preferred to have a man as a doctor. Most of remaining men, and 31% of the women, did not mi whether their doctor was a man or a woman. 16% the women, but less than 1% of the men, preferre woman doctor.

All informants were asked how they came to cho their present doctor. Only 1% gave the sex, religi or nationality of their doctor as the reason for th choice In 1% of cases he was a relative, friend business acquaintance A further 2% had first cal him in an emergency 23% had, as it were, inheri the family doctor 9% had taken over the husban or wife's doctor on marriage. 14% said they had re on recommendation These six groups, amounting half of the informants, may be said to have had so knowledge of their doctor before they chose him.

The remaining half gave reasons which sugge little knowledge of the doctor either directly or hearsay 15% chose the nearest or most convenien situated doctor, 4% took the only doctor availa 22% accepted the successor to a practice Most of rest could not remember how they chose their doctor

Changing Doctors

Informants were asked whether they had changed th doctor since the health service began, and if so reason for the change From their answers it is estima that the annual rate of changing doctors is abou per 100 adults in the service, but that four fifths of th changes are due to movement either of the doctor or patient The next largest group of changes, but o a tenth of all changes, is due to the patient's dissa faction with his doctor or with the treatment receiv Thus changes due to dissatisfaction amount to abou per 1000 adult patients in a year Smaller proporti of the changes were due to a wish for a doctor clo at hand, a wish to have all the family under one doct and a preference for a doctor of a particular sex, mai for a woman doctor

Patients' Opinions

When asked whether they thought the attention th received from their doctor was better or worse since health service started, only 16% of those on a docto list thought there had been any change Half of th thought it had changed for the better and half for worse Better attention meant in the main lon consultations and greater interest shown by the doct Worse attention meant the reverse About a third those who thought the attention was worse felt that doctor was not interested in them Rather more th another third felt that the doctor was too busy, had many patients, or, as one patient put it, was "too rea with the pen." Another appreciable group complain of having to wait in the surgery or that the doctor wo not call

Informants were divided into four groups according whether they were former panel or non-panel patie and whether they still had the same doctor as bef the health service or a different one In both group former panel patients a higher proportion thought attention was better The highest proportion, 1 was among former panel patients who no longer had same doctor In the groups of former non-panel patie more people thought the attention was worse rath than better, and the group of former non panel patie who no longer had the same doctor had the high proportion, 12%

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* Standard error ± 0 3%
† Standard error ± 0 7%

SUMMARY

Of a sample of 7027 adults interviewed in February and March 1952, 97·7% said they were on a doctor's list under the health service, 95·7% relied solely on the service but 2·0% also used private practice. Of the remaining 2·3%, 1·7% were using or would use private practice while 0·6% would probably make use of the scheme if they became ill.

About half the reasons informants gave for choosing their doctor suggested that they had little previous knowledge of him either directly or by hearsay.

It is estimated that the annual rate of changing doctors is 7 per 100 adults in the service. Movement of patient or doctor accounts for four-fifths of these changes. About 7 changes per 1000 patients are due to dissatisfaction with their doctor or the treatment received.

84% of the informants thought that there had been no change in the attention given by their doctor (he was not necessarily the same one) since the N.H.S. started. Of the 16% who thought there had been a change, 8% thought they received better attention, 8% worse.

THE DISABLED TUBERCULOUS

Hostel and Workshop

The old chronic tuberculous patient with bacilli in his sputum, little social conscience, and no fixed home is an unfortunate person, besides being a risk to those who befriend him. He is apt to go short of both food and rest, the two chief essentials in his treatment. If he is in lodgings, and poor, he may economise by eating out as cheaply as possible, and he may also hesitate to spend too much time on his bed lest his landlady should suspect his trouble. If his only home is the common lodging house, he is usually not allowed in his cubicle between 8 A.M. and 8 P.M., and if, at night, he finds the house full he may have to tramp to another district to find a bed—a thing that often happens in large towns in winter. Dr W. Hartston (London) and Dr J. F. Macgregor (Middlesex) who draw attention to these hardships,[1] say that the homeless consumptive, especially if he is unable to work, or has diabetes, is doomed to a falling standard of care and nourishment, and they describe how his difficulties may be eased by the tuberculosis hostel.

Both London and Middlesex have taken advantage of the powers extended to local authorities to establish such hostels, which, as Hartston and Macgregor point out, not only increase the comfort of patients with advanced disease but also help to relieve congestion in chest hospitals (for few superintendents can steel themselves to discharge such patients on to the streets, and almoners can seldom find lodgings for them). Moreover, by providing alternative quarters for an infective uncle or grandparent, the hostels reduce the risk to other people, and especially to young children, who are living in the same household.

HOSTELS IN ACTION

The first hostel used by the London County Council for the tuberculous was opened at St. Albans in February, 1951, and was privately run. It had beds for 40, and during the time it was used for this purpose had an average of 36 men in residence each week. Later in 1951, however, it was found convenient to establish a hostel in Islington run directly by the L.C.C., and in September, 1952, some of the patients then in residence at St. Albans were transferred to this new hostel, while the rest went as temporary guests to Preston Hall.

The two roomy houses at Islington have so far survived demolition in an area scheduled for L.C.C. rehousing, and are not perfectly suited to their purpose, having many stairs; but they are airy, light, and welcoming. The walls of the rooms, painted a kind of golden toffee-colour, catch whatever sunlight is going and diffuse it. The bedspreads, too, are yellow, and the spacious bedrooms are not crowded, either with beds or furniture. Two or three beds to a room, set well apart, are the rule; but there are a few single rooms for those who prefer them; actually there are not many who do, for people liable to be ostracised are apt to favour a bit of company. Each man has a wardrobe of his own, simply but well made in natural wood, and a roomy bedside locker. He can use his bed at any time he likes, and many of the residents take an afternoon rest as a regular thing. A large billiards room equipped with a full-size table, and a plain but comfortable sitting room, both open by french windows on to a long balcony, overlooking the garden. Though the garden itself is disappointing (being at present rough and overgrown) it contains two well made chalets which are much prized by those residents to whom they are allotted; electric light and electric radiators make them comfortable even in winter.

A warden and his wife look after the residents and cook their good meals. The warden is a trained caterer and his wife has the maternal qualities the job demands. The dining room, plainly but pleasantly furnished with chairs of good design and several small tables, opens off the kitchen. There are separate sinks for washing up the crockery of patients and staff, and of course separate crockery. Soiled linen and blankets and bedding are disinfected by the borough health department before being sent to the laundry, and every newcomer has freshly laundered blankets given him from the linen cupboard. Bathrooms and wash basins are ample in number, and each hostel has a sluice for sputum disposal, fitted with a device for delivering a measured quantity of disinfectant into the man's pocket sputum flask.

The average number of men in residence each week in this hostel is 36. They may be any age, but there are just about as many between 40 and 60 as there are over 60; very few are under the age of 40. Since there are two houses (though they are joined, and have communicating doors at various levels) it has seemed a good plan to sleep the older men in one half and the younger ones in the other, and this suits both.

In July, 1953, a second hostel was opened by the L.C.C. at Fulham. This is run on much the same lines as the Islington hostel, and is also situated in a roomy private house—a very agreeable one, with a large and well kept garden, looking across a sports ground (and giving a fine view of the football matches played there). In many of the rooms the large windows stretch almost from floor to ceiling. Here too the equipment is plain and good, the food appetising, and the warden and his wife well suited by nature and acquirements for the job. This hostel can take 25 men.

MANAGEMENT

The residents in these hostels pay for their lodging according to their means, on generously assessed terms, but naturally the hostels are not self-supporting. Since, however, they have been established in existing houses and equipped simply (though well) they have not been excessively costly to set up. Hartston and Macgregor point out that though a hostel taking 40 or 50 may be more economic to set up than one taking 20 (which they consider to be the optimum) it is likely to be less successful because the staff will be too busy to make friends with the residents, who in turn—like the residents of other boarding houses—may then split up into hostile cliques.

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[1] *Tubercle*, 1953, 34, 179.

The original idea was that one hostel should be for men going out to work, and the other for those not fit to do so, but as it turned out, very few of the residents were fit for work the demand comes mostly from those who will never be able to work fixed hours again Some pick up small sums selling evening papers, but this is hardly an advantage, for it may cause them to leave their hostel. His bed once booked in a common lodging-house, a man can go in at any hour (after opening-time) he likes, but hostels, staffed for daily living, have to have a closing hour There are few other restrictions the men come and go as they please during the day, and many of them go out. The aim of protecting others would perhaps be better fulfilled if some light occupations could be provided for them in the hostels. Lending libraries give plenty of discarded books, and billiards, and no doubt cards and dominoes, are provided; but few of the men seem to be readers, and games can pall An occupational therapist might be able to offer them more creative pursuits

A general practitioner acts as family doctor for each of these hostels, but if any of the residents need hospital treatment the local chest physician takes responsibility for them, and he has been given extra beds to help him to do so. There is naturally a fairly high relapse-rate. Applications for a place in a hostel come mainly from hospitals and chest clinics, and are sifted by the responsible officer of the local authority This is only fair, since applications come from a wide area, and there are not beds for all who come

Experience has proved that the hostels are needed, and are doing useful work at small cost The demand, in fact, is presumably far larger than the accommodation so far provided For a fairly dense urban area Hartston and Macgregor estimate it to be 5 hostel beds per 1000 tuberculous males.

A WORKSHOP FOR THE HANDICAPPED

A different type of help for men handicapped by tuberculosis is the sheltered workshop provided by Middlesex County Council at Tottenham Here a Civil Defence building, put up for decontamination of gas casualties in the late war, is being used to employ such men In every case the chest physician has given the opinion that they are not fit to do a full week's work The men are trained at the workshop as carpenters, joiners, and cabinet makers, and in six months become fairly skilled workers They are kept fully occupied by orders for equipment from the various county-council departments The standard of joinery is high, and the finish of the work both good and agreeable The main workshop is rather low, but light and airy A five-day week is worked, and of the 41 men now employed 2 began by doing six hours daily, but now do eight hours (a forty-hour week), 3 do seven hours, 23 six hours, and 13 four hours There are also 8 or 9 men in training, on grants from the Ministry of Labour All the trained men are paid a full week's wage at the minimum trade union rate for the job, even if they are able to work only a four hour day This frees them from any need to seek public assistance grants, and since their work must in any case be subsidised from public funds, it seems civilised to subsidise it in this dignified manner, which neither puts the man at a disadvantage with his fellow workers nor multiplies the activities of official departments Nevertheless it places a heavy financial burden on the local health authority It can be argued with some justice that the workshop is intended for men who will eventually be able to work 8 hours a day in sheltered surroundings and that there are plenty of such men about Many, however, live so far from the workshop that the journey would be too much for them clearly a workshop of this [illegible] only serve a limited area. Those admitted to [illegible] are carefully selected by the chest physician from patients—most of them still sputum-positive—who have completed their treatment but are no able to undertake full-time work, anyhow for some They are fit, however, for employment under conditions, and not at high pressure, and many of within six months or a year become able to work 40-hour week and keep well The selection of patients is not easy, of course, and some of the not progress as well as was expected. A few fit for more than 4 hours' work a day, and it might argued that sheltered employment was never for these But their state of mind and general improve, and they are better off doing part-time than they would be suffering idleness and boredom the lower standard of living which are the lot of those National Assistance grants. Those who work all day are no better pleased than the labourer in the parable to see those who have done less getting the same pay and human nature being what it is, there is a tendency for men who are getting full-time pay for working half time to show no enthusiasm for working longer hours for the same money It is difficult to find an ideal solution to the problem The answer seems to be additional work shops of the type that cater only for part-time employees but the establishment of these must naturally take second place to workshops for those fit for full time work

The reablement and sheltered employment of people handicapped by pulmonary tuberculosis deserves to be considered as responsibly as treatment of the disease it is part of the general management of patients suffering from tuberculosis, not a service that can be run at a profit The heavy financial subsidy brings valuable returns, none the less, for sheltered employment keeps infectious patients from having to seek employment in the open market, where they are a continual source of danger to their workmates, and—by raising the standard of living—helps members of their families to resist infection

The Tottenham workshop certainly reflects great credit on Middlesex It was begun in a small way in an occupational therapy unit, where it struggled on in awkward quarters until it had proved its worth When the county council provided the present workshop, in 1948, the plan was to employ 24 carpenters, and two additional groups of workers—shoemakers and sempstresses—who could have been accommodated in the same building Though this scheme was never approved the woodworking scheme was extended, and the workshop is now allowed to take up to 52 carpenters and cabinet makers

The relapse rate among these men is high, as might be expected in view of their serious disability but most of them return to work again after further treatment

Of 69 trained and employed during the four years between Sept 1, 1949, and Aug 31, 1953, 49 are still employed in the workshop, 1 has graduated to full time work in open industry, 3 are in other employment (1 in his own business, 1 as a male nurse, and 1 in a Remploy factory), 6 have left because of permanent sickness, 4 are in hospital, 5 have died, and 1 has been discharged as unsuitable.

Of the 49 now employed, 10 have been in the workshop for over 4 years Only, 14 have had bouts of illness lasting more than 4 weeks Their sick pay is generous. they receive full pay for the first month, and full or half pay, according to need, for the next 3 months, after that they go on National Health Insurance

In one respect the incidence of illness among men is reduced. they show none of the depres anxiety, and apathy so common among disabled men they are *not* employed. Much of the credit for the hap atmosphere of the workshop, as well as for the standard of craftsmanship, must go to the instruc manager, Mr W R. Osment

The Widdicombe File

V FORWARD MARCH

DEAR PETER,

I am anxious to come up and talk surgery Can you put me up next week ?

Since we last met I have bought a *forty-acre* moor land farm in Devonshire from which I am writing to you today I have two more years on the Hospital staff When I retire I hope to retain enough private practice to pay the rent of my flat and consulting rooms for another five years. Meanwhile I intend to spend my holidays and most of my weekends down here preparing a home in which to spend my dotage.

Conditions are primitive. The farm house has three rooms on the ground floor, tiled, and heated by a huge open wood fire The stair to the upper storey is more like the ladder it replaced than a real staircase The basins in the bedroom and the bath in the scullery are filled from jugs, and the waste runs into the yard The lavatory is an outside earth closet Water is pumped by hand from a well. Lighting is by paraffin lamps and candles.

Living under these conditions is Spartan but reassuring I know that every device ministering to my needs has been tried and tested by centuries of constant use. The walls will stand any shocks short of atomic explosions. There are no drains to smell or get out of order There are no pipes to freeze in winter Coal strikes will leave me undismayed. Electric failures will not affect my cooking or my illumination My water is safe unless I foul it myself and it never stinks of chlorine. My milk comes from a cow rather than from a tank in which the yield of two thousand cows, refrigerated and chemically protected, has been carried by lorry from country to town, graded, sorted and bottled and sent back again to the country My eggs were laid by a European hen My butter owes none of its colour to dyes and none of its freshness to preservatives I shall spend the next five years bringing the house up to date, but shall I be any better off when I have finished ?

Science has advanced more in the last twenty five years than in the previous two thousand. So we tell ourselves, but sometimes when large transport-planes drone overhead, disturbing our sleep and dropping blocks of ice on our greenhouses, or when political vans parade down our streets bellowing like sea-lions at feeding time and making work and even thought impossible we wonder if advance and progress are necessarily the same thing The old fountain pen which we filled by unscrewing the top and running in ink from a glass filler never leaked and would write for a week without replenishment the modern balloon reservoir pen spoils all our waistcoats and will seldom write more than five or six hundred words without refuelling The pre-war motor-car was not so fast as the black beetle that has replaced it, but it went and went on going for years, and it had two accessories that were worth more than all the gadgets of today—a hand brake that really held it on a hill while one wheel was jacked up for a tyre change and a hand throttle that allowed the driver to adjust the engine to a nice tick over and to rest his tibialis anticus on a long drive Even the wonders of modern anæsthesia pall at times, and the surgeon wishes he could go back to the bottle and mask and an abdomen to which the guts could be returned at any rate till the peritoneum was closed.

* * *

I am proposing to visit you because I want to see you do some prostates. In London we all do the retropubic operation In the North you all do the transvesical But in both places each surgeon has his own modification of the Millin or the Wilson Hey How much is there in all this ? How much better are these modern methods than Horner s operation as performed by Freyer ? Sidney Macdonald did the Freyer operation unvarnished and unmodified till he died and I doubt if any surgeon today has a lower mortality or gets better functional results You now work by direct vision and use diathermy and you probably have a cleaner and drier field at the end of the operation. Do you think there is much in it ? You poke your catheter down the urethra from bladder to meatus and think you are keeping out bacteria thereby ' Kind hearts are more than coronets, and simple faith than Norman blood ' You are able to close the bladder ; but is that because you do a better job than Freyer or because you knock hell out of your house-surgeons ? In Freyer's day they slept at night now after a urological afternoon they must abandon sleep and girl friends till the last clot has been washed out. You no longer fear to operate in acute retention, and that is a real advance but surely blood, chemo therapy, good anæsthesia, and good sales talk will account for the rest.

* * *

Surgery has certainly changed in our time When I came to hospital, the last of Lister s pupils had just gone off the staff, but antisepsis was still a religion and germs were still looked on as evil Every ward had an alcove in which were stored antiseptic solutions and dressing materials Glass cisterns containing solutions of carbolic acid 5% perchloride of mercury 2% lysol 2%, and a saturated solution of boric acid (coloured pink blue yellow and white) stood on the shelf and below them were glass jars containing pads of sterile gauze iodoform gauze and sal alembroth gauze (white, yellow, and mauve) Ward dressings formed a great part of our work Clean stitched wounds were dressed daily If they remained clean the stitches were removed after a fortnight ; if not they were put on to four hourly hot boracic fomentations after removal of alternate stitches Septic wounds were dressed morning and evening, and sometimes four hourly Tubes, of which there were often several, were removed and boiled at each dressing the tube track was syringed with an antiseptic lotion till it was clean and the tubes were then reinserted

In the theatres gowns and towels were sterilised in the autoclave, but instruments, after being boiled were kept in an open tray of lysol Some surgeons worked with bare hands and scorned masks, but the majority wore masks and boiled gloves. The seniors of that day were expert anatomists but having served a long apprenticeship in the dissecting room and having been denied access to beds, except during holiday time till they got on the senior staff, they had never acquired skill with their hands. With two exceptions, the men on the surgical staffs of the London teaching hospitals up to the first world war were bad operators by modern standards —far inferior to the surgical registrars of today

You joined the R.F C while a student and when you came into the wards in 1919 you found a very different picture Four years of war had shifted the emphasis in wound infection from the attack to the defence, from the bacteria to the resistance of the tissues In the theatres dry sterile materials were the rule and dry sterile gloves had replaced wet ones. Emergency work included acute appendices and the accidents of dock and factory but those commonplaces of pre-war ' take ins, the strangulated herniæ the extravasations of urine, and the late appendices admitted with general peritonitis, were already becoming rare Most of the patients coming from the theatres to the wards had clean stitched wounds covered with sterile dressings over which were many layers of sterile wool and voluminous bandages, and these dressings were retained till the stitches came out The coloured lotions and the coloured gauzes had disappeared and the only antiseptics in common use were flavine and Dakin s solution

A younger generation of surgeons, trained to operate in the casualty clearing stations, and taught to look on clean dissection, gentle handling, and accurate hæmostasis as the chief safeguards against infection, had taken over and were setting a new standard Rapid operating was no longer regarded as the hallmark of surgical skill, but on the other hand an operation lasting much over an hour was a thing to be avoided Anæsthesia was emerging as a specialty, but pink ears and a relaxed abdomen were still the exception rather than the rule

* * *

Nowadays we are a bit too complacent about surgical advances From 1870 to 1915 things really did move Victorians imbued with the spirit of the Elizabethans, gay adventurers armed with weapons of a potency hitherto unknown, hacked their way through an unexplored jungle to discover lands of rich promise From 1915 to 1935 their successors cultivated the land so hardly won, brought it into production, and extended its territory Since 1935 further advances have been made we have seen a steady improvement in the scope of surgical enterprise, in the increased safety of surgical operations, and in the diminution of postoperative morbidity, but I don't think that we surgeons can claim any of the credit The surgeons of 1920 were better than the surgeons of 1910, but I don't think that the surgeons of 1953 are any better than those of 1920—than men like Gordon-Taylor, Charles Saint, John Fraser, Richard Charles, and many others who worked behind the lines in 1917 and 1918 On the other hand, surgical environment, surgical method, surgical equipment, and surgical auxiliaries have improved out of recognition Continuous intravenous administration—the basis of planned resuscitation and of all supportive and postoperative therapy—was introduced in 1925 only, and reached England in 1930 Gastric suction appeared about the same time, and intestinal decompression followed later The physiological outlook that abolished purgation and starvation, that brought the study of fluid and salt balance, and that taught the dangers of postoperative immobility, was a result of the break with tradition and the rational outlook that came of the first war Chemotherapy first appeared in 1935, and was not in effective use till 1940, while penicillin came three years later

The position of surgery today depends more on the improvements that have taken place in anæsthesia than on anything else Men like Macewen, Trendelenburg, and Arbuthnot Lane advocated operations on the lungs and heart half a century ago, and Sauerbruch played with his differential pressure chamber thirty years ago, but it was not till the advent of closed circuit anæsthesia and controlled respiration that pulmonary and cardiac surgery became a reality

Just watch that patient on her way back to the ward after a mitral valvulotomy (How I wish that our thoracic surgeons, brilliant and lovable colleagues as they are, were not so careless with their language We should shudder if a gynæcologist talked of cæsariotomy, or a physician of renitis, yet we allow this bastard offspring of two noble languages to defile our literature "Valvulotomy"—ugh! "Valvotomy"—even worse The valve is one of nature's inventions applied by man to his own uses from the earliest times, and the Greeks certainly had a word for it Epistomion has a pleasant ring about it, but I am told at Balliol that it does not occur in the classical period Sandon is better Let the International Society of Thoracic Surgeons, when they next meet in Buxton, Stockholm, Locarno, Hot Springs, Santa Barbara, or Buenos Aires, table a discussion on the relative merits of epistomiotomy and sandotomy as the first item of their agenda, and, having made their choice, apply for readmission to the ranks of the educated)

We shall have to run down the stairs to catch our pat[illegible] the bottom of the lift She looks as if she had just woken from a pleasant sleep Her eyes are brigh her breathing is quiet, her skin is warm and dry, and sl has just started to chat to the nurse who is seeing h back to the ward Her wound is covered only by a str of gauze held in position with a few bits of strappin Soon she'll have a cup of tea Tomorrow she'll be sittı in a chair In five days' time her stitches will be ou and in ten days she'll go home Yes Peter, surgery h changed in our day

* * *

Personally I'd say that the most important improv ments of the last five years have lain in receding fro the advances of the previous ten The radical surge of malignant disease of the pancreas has been foun except in ampullary growths, to shorten rather tha prolong life and to make the end more miserable Vag tomy, the vaunted cure of peptic ulcer five years ag is now a thing we had rather not talk about The surgic removal of prolapsed intervertebral discs has bee found, on the whole, less satisfactory than treatme by manipulation or by a spinal brace Sympathet operations for hypertension have proved unnecessa in early cases and useless in late ones, and they survi merely as an occasional palliative to relieve intolerab headaches and failing vision Shunt operations for port hypertension have hitherto escaped debunking, but the are in urgent need of it

But ground is also being won that will never be lo again The surgery of mitral stenosis, the surgery coarctation, the grafting of arteries, these will remain and next week when we come back from the prosta session to a good dinner and a glass of port we sha remember others At any rate we shall thank our sta that we have spent our lives in a job that can never standardised or planned on mass production lines.

Your old friend,

DANIEL WHIDDO

Parliament

QUESTION TIME

Myxomatosis

Replying to a question Mr G R H. NUGENT, joint parli mentary secretary to the Ministry of Agriculture, said th in the past four weeks 5 fresh outbreaks of myxomatosis wild rabbits had been confirmed. There were now 3 centr of infection in Kent, 2 in East Sussex, 2 in Essex, and 1 East Suffolk The most recent outbreaks were in Esse East Suffolk, and Kent There had been no appreciable loc spread of the disease at the existing centres of infectio About 800 rabbits were known to have died of the disea since it was first reported More infected rabbits might hav died in their burrows either from the disease or gassing

Mr SOMERVILLE HASTINGS What are the latest ideas to how the disease is conveyed? Is it by birds or by huma beings, or only by direct contagion? Mr NUGENT I thin it is probably conveyed by direct contact between the rabbi and by insects—probably to some extent by birds as wel but mainly by insects in the spring and the summer

Mental-hospital Nurses and National Service

Replying to a question, Mr H. A WATKINSON, parli mentary secretary to the Ministry of Labour and Nation Service, said that student nurses in mental hospitals we not exempt from National Service, but their call up could deferred until they had completed their training

Sale of Condemned Meat

In answer to a question, Major GWILYM LLOYD GEORG the Minister of Food, gave the following summary of th revised conditions for sale of condemned meat

> Condemned meat and offals bought at auctions from Govern ment slaughterhouses must now be processed boiled, or sterilis before re sale Where the meat is re-sold to a retailer for anima feeding or to a processor the liability for processing boilin or sterilising must be included in the contract of sale Sellers o raw condemned meat and offals must inform the medical officer o health in the area where the meat is delivered of the names an addresses of the consignees

In England Now

A Running Commentary by Peripatetic Correspondents

GETTING out of the United States is so absurdly simple, compared with getting in, that it almost gives the impression that nobody cares. To get *tecsticards* across the Atlantic requires quite a lot of effort. Passport (with photos of course), vaccination (certified) visa (more photos) a personal interview and a lot of questions connected with MacSomebody's Act,' monetary arrangements and so on Two lots of immigration officers came on board in the St. Lawrence River and took a real interest in our dossier With characteristic kindness and clarity they wished us a good trip and *cautioned* us on no account to part with the visa papers until we left, implying that these represented our only hope of escape. It did *not*, however work out that way at all. Warned by the shipping people of something formidably called a ' sailing permit,' we had visited the income-tax offices and with courteous help filled in a lot of details revealing our relative lack of earning capacity in the States. The time of departure arrived. This was the moment when another kind official would surely scrutinise us for the last time ask after the trip and with some ceremony remove our visa papers and sailing permits. So when the baggage had been sent on its way from the taxi to the ship (and no examination of that either) we looked around for the aliens this way" notice There wasn t one A dock-side cop suggested that our passport business would be taken care of on board so on board we went. There was still no sign of the U.S government The chaps (and girl) in the purser s office were quite amused. " Oh no ! " they said, ' *they* aren t interested any more. So our sailing permits went into the garbage box in the cabin (sorry—British ship—wastepaper basket) and the visa papers into ditto after the purser s assistants had ripped them out of the passports. It really hurt a little Nobody cared.

The philosophy is probably simple and logical, like most things in the States. No decent sort of person could possibly want to leave such a pleasant land and nothing must be done to hinder the departure of the other sort. So the absurd traffic light at the end of the dock changed from red to green and the big ship backed out unailed exactly at the promised sailing time Not even the first respectable cup of tea for five weeks quite removed the feeling of anticlimax. Perhaps MacSomebody-or-other should give the matter a little attention.

* * *

I have lately been able to neutralise two nuisances of modern life, and as a small contribution to sociology if not to science I have decided to publish my method

A so-called friend thinking no doubt to confer riches upon me in the modern manner lately divulged my name and address to a football *pool* The result has been a monotonous and unwanted weekly envelope packed with esoteric forms. I examined the first packet but found the problem beyond my mathematical capabilities All subsequent envelopes went to swell the family salvage collection.

My small son is undergoing the early processes of education Inheriting no doubt paternal tendencies, he was advised or more likely instructed, to practise writing (both letters and figures). This means that someone and there is an obvious choice, has to rule paper for him. With a chipped ruler this is at best, a tedious operation.

An idea of staggering brilliance brought together these two nuisances. The football pool forms provide a ready-made page regularly divided into lines, columns, and squares eminently suitable for guiding the letters and figures of a wavering childish hand. And who knows if I ever post back one of the completed forms, it might yet fulfil its intended destiny

* * *

Rabbit-keeping is very traumatic to the parent. Our numbers vary from day to day, though my two children merely own two males (Cottontail and Parlicoot) The total group, two harlequin Dutch a white angora, a rabbit-coloured angora, a grey fierce plushy type, and my own two Belgians increased in two weeks by 16 babies, but an epidemic has appeared in the three-*month-old ones. They just fade, and I,* as a doctor in the house, am shown the corpse in the incinerator I have not done a post-mortem and I have listened gravely to all the ætiological views. Our authority up the hill on the small holding says it is poisonous weeds, and the youngest scapegoat is blamed My friend in general practice says it is overcrowding, and the man in Boots veterinary department says avitaminosis (B) Rival rabbit-owners accuse one another of neglect, and wilful starvation. My two children madly increase the living-space, provide lashings of water, and obsessionally sort the bunches of fresh grass for poisonous weeds.

In spite of all this, Parlicoot was obviously sickening when we returned from our evening session. He was cold not eating respirations shallow and slow, had lost his plump glossiness and felt like a bag of bones. After consultation with my senior colleague we plumped for a virus infection, and, failing all else introduced five minims of topical chloramphenicol orally Within three hours we heard a reassuring grind of teeth from the hutch at the foot of our bed We gave him two more minims for luck and in the morning he actually licked it up He convalesced, more or less, in my son s arms and after 18 hours had an ecstatic reunion with Cottontail. On Thursday the rabbit-coloured angora was dead, and his brother comatose. We put him on to chloromycetin at once. After each of the first two doses he regained consciousness, but during the third dose he lay in opisthotonos and apparently died As I left my daughter rushed up Mummy, the children say the one in the incinerator is moving ' I shut the car door on myself deliberately Grandly, but with a craven heart, I said ' Tell them I say he is dead ! '

Parlicoot was a bit inflated last night. We feared liver damage with ascites, but it was only wind

* * *

If you dine at any of our more expensive restaurants you will almost certainly find that the waiter will bring your change on a plate The plate is usually taken from one of the tables, and after you have clawed the coins from the slippery surface and left an appropriate residue for the waiter you will see the empty plate duly restored to the table The experience always makes me a little uneasy about the plates I have used.

At a hotel where I dined last week I plucked up courage to mention the matter to the waiter The man was evidently a foreigner and for a few moments he looked puzzled. Then the kindly light of reason shone from his eyes and he exclaimed—to the great delight of the guests at the tables nearby— Ah yez, now I understand Zee plate—zee jairms—veree bad Yez, I send 'im back to kitchen for wash ! '

My objection to the practice is æsthetic. I am prepared to hear from some *learned* bacteriologist that coins are no dirtier than the waiter's hands—and no cleaner Indeed it might turn out that coins provide a poor culture medium for bacteria. Perhaps the minute amounts of metal combined with the animal proteins of sweat, sebaceous secretion, and epithelial debris lying on the surface are ultimately fatal to most micro-organisms. But I still think that if the waiter were to drop a handful of coins into the bacteriologist s broth he would send it back to the kitchen

* * *

When my five-year old daughter came home from school singing the following song I realised that modern education has not yet caught up with the National Health Service

Miss Polly had a dolly who was sick, sick, sick
So she sent for the doctor to come quick quick quick
The doctor came with his bag and his hat
And he rapped on the door with a rat tat tat
He looked at the dolly and he shook his head
He said Miss Polly put her straight to bed "
He wrote on a paper for a pill, pill pill.
" I'll be back in the morning with my bill, bill, bill

At the end of the song she looked at me with a puzzled expression and said Mummy, do people have to *pay* doctors ? '

Letters to the Editor

THE TELESCOPE IN MEDICINE

SIR,—More than ten years have elapsed since John Ryle became the first professor of Social Medicine in this country Yet we still find the terms Social Medicine and Public Health being used as though they were synonymous The two subjects are frequently linked together for teaching purposes and their subject matter has much in common There is, however, a fundamental distinction between them, for Public Health is essentially part of medical practice whilst Social Medicine is a highly specialised branch of medical research

It is not surprising that in his short term of office Professor Ryle should have failed to produce a convincing definition of the subject For he was setting out to break new ground and had been saddled with an awkward title If, however, contemporary workers in this field allow the profession to assume that they are merely attempting to widen the horizons of medical practice they may endanger the future development of that part of medical theory which is concerned with the study of causative agencies

The study of ætiological factors in medicine is a vast subject In the remote past it was the sole prerogative of clinicians, but in recent years the most valuable contributions have come from the laboratories For, unlike their predecessors, laboratory workers possess tools which have enabled them to identify in particular diseases the (usually minute) causative agencies which are common to every case By concentrating on these they have also uncovered two facts of the greatest importance to medical theory First, that the universal agencies are rarely, if ever, the sole cause of disease, and second, that not all the persons exposed to their action become ill It follows that causative agencies exist which are not common to every case of a particular disease

At first sight this suggested that every case of disease was unique , and if clinical work had not already shown that a significant proportion of affected persons had other things in common the theory of uniqueness might have been accepted As it was, many long suspected genetic and environmental associations had been confirmed by clinical research and new ones were being added to the list of suspects To discover the nature of these accessory agencies new lines of ætiological research were developed In this field also the experimental method proved remarkably successful and to this we owe, for instance, the theory of innate and acquired immunity to infection We must, however, face the fact that there are in the accessory class two types of causative agencies—those which can be investigated in the laboratory and those which cannot The former resolve themselves into the study of certainties and the latter into the study of probabilities

This distinction is an extremely important one, because to make *precise* estimates of probabilities it is not enough to note that certain types of person more often present themselves for treatment than others *That is to say, the ætiological problems which do not lend themselves to experimental investigation also lie outside the usual range of clinical investigation* It is this challenge which is today being met by the new departments of Social Medicine Their methods involve the isolation of groups or populations defined by the genetic or environmental influences which it is proposed to study The behaviour in certain respects of these and control groups is then followed and significant co variants are identified by making statistical comparisons

The division between Social Medicine and Curative Medicine, and the essential links with group studies and statistics, probably account for the present tendency [illegible] it with Public Health For the older and better known subject is concerned with prevention rather than cure it serves the community rather than individuals, and it involves the collection of statistics It is not, however, called upon to use statistical methods as a research tool

Once it is recognised that the new subject is not concerned with medical practice but with the underlyin theory, its position vis à-vis other branches of medicin can be more clearly seen Clinical Medicine and Public Health then appear as partners, the former providing a curative service for individuals and the latter a preventive service for the community Behind them stand the Experimental Medicine and Social Medicine teams, each providing a quota of facts and theories on whic the practitioners base their respective policies

Needless to say, out of the practice of medicine new knowledge is constantly emerging, and in the workshops of medicine many practitioners are employed Nor is this free interchange of work and ideas the only reason why it is difficult to keep certain distinctio clear In medicine, above all things, the provision of service with wide and ever-extending ramifications ha had to take precedence over everything else So incessant has been the demand for practitioners that it is only comparatively recently that the profession has been able to carry whole time research-workers The original corpus of medical theory was created and maintained by physicians and surgeons whose busy practices d not prevent them from making careful studies of thei material and recognising essential links between their diverse observations The clinician still has a unique rôle to play in medical research, but today it is possible to supplement naked eye observations with those made with special instruments On the one hand there are the microscopic methods of the laboratory workers and on the other the telescopic methods of Social Medicine.

The latter has so many things in common with astronomy—the wide range of observations, the focus on distant objects, the rigidity of the universe observed, and the dependence upon mathematics—that one is surprised that no pioneer ever drew the analogy Had he done so the founders of the Oxford chair of Social Medicine might have hesitated before selecting their title The one they chose obscures that fact that th subject is a branch of fundamental research and (by suggesting a social service) has given rise to false expectations It would indeed have been better to have done as Cambridge has and omitted both the word social and the word medicine But the Cambridge title, Human Ecology, is still unsatisfactory Its implications are to wide , it fails to show the relationship with medica science, and it gives no indication of the basic methodology Since the subject is solely concerned with ætiological problems the term ætiology should appear in the title, qualified—for it must be distinguished from experimental and clinical studies—by the adjective statistica

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ALICE STEWART

LACTIC ACID IN THE TREATMENT OF OSTEO-ARTHRITIS

SIR,—Though Mr Waugh (Nov 21) and Dr Vergett (Nov 28) have made some valid criticisms of the conclusions reached in my paper, I do not feel that they are such as to convince me of the value of this remedy. Mr Waugh is of course correct in saying that what the trial proves is simply that among miners and wi the technique used, lactic acid has no therapeutic actio in osteo arthritis Nevertheless, while recognising Mr Waugh's much wider experience of the technique involved, I would question whether osteo arthritis in miners really responds so very differently from the same disease in others If this is so, it is surprising th negative results were also obtained by Desmarais in t ath area where coal mining is likely to be a less frequent ource of livelihood

Mr Waugh's criticism of the absence of statistical nformation on the value of physiotherapy is certainly ully justified, but it is hoped that work in progress at resent will remedy this deficiency

Dr Vergotte has implied that physiotherapy may in ome way neutralise the effect of lactic acid. If this is o, the results of a trial comparing untreated patients ith those receiving lactic acid should, as he suggests rove very informative Until he has produced uch results, however we must, I think consider the alue of lactic acid at least doubtful and certainly mproved

Department of Rheumatism Research
Manchester University
J S LAWRENCE

OPERATING THEATRE INFECTIONS

SIR —After reading the report by Dr Sevitt and your leader (*Nov 28*) *followed by the excellent letter by* Mr Gissane (Dec 5) I considered that pharmaceutical manufacturers might be able to offer some useful advice, backed by experience in maintaining near-sterile conditions in an operating theatre The task of maintaining rooms with air of very low bacterial content has been carefully studied for a number of years by pharmaceutical manufacturers I would point out that any powders or liquids which cannot be sterilised in their final sealed containers must be packed under aseptic conditions followed by bacteriological control Contaminated batches are naturally discarded and packing is carried out in rooms larger than operating theatres with more people working in them So the problems are by no means insoluble

Mass-production packing of thermolabile drugs, such as penicillin and streptomycin, under strict aseptic conditions, presents difficulties similar in many ways to those of the operating theatre In each case a surprisingly large number of persons must enter and work in the "sterile area." There is much coming and going with many trolleys and trays of bottles, doors are opened and closed, and much delicate work is carried out under strict aseptic conditions with sterile instruments in gloved hands. Sterile clothing complete with mask head-dress, and boots *is donned on entering* the sterile area.

Pharmaceutical manufacturers rely on positive pressure in the sterile area, with rapid air changes. Thus all draughts are away from the sterile area. All surfaces (floors, walls and benches) are capable of being washed with antiseptic solutions. Dust-harbouring shelves and ledges are avoided, especially above bench level thus avoiding falling dust particles. Lights are built into ceilings. The positive pressure is produced by means of a fan blowing filtered air of very low bacterial content into the room at ceiling height This air is drawn from outside the building preferably above roof height, and passes through a filtration unit. It leaves by slit ventilators with hinged flaps which act as valves should the room pressure be reduced by say the opening of a door Thus, airborne dust cannot gain access to the area

The most important part of this scheme is to ensure that the air blown into the area is virtually bacteria free at all times. It has been recently shown by Sykes and Carter[1] that air of very low bacterial content can be produced by simply passing air under controlled conditions through filters of oiled "Fibreglass" or cotton fibre These filters are commercially available and under suitable conditions up to 99% efficiency is claimed.

The only sources of infection from outside the area are on the persons of the workers, who wear sterile clothing, and on the trays of bottles, which are fresh from the steriliser The main difference in this analogy would seem to be that the patients and the trolleys are so difficult to sterilise!

Ultraviolet light has been used by some manufacturers as an added precaution The sceptic might remark that it is only to impress visitors to the factory The use of ultraviolet radiation in the air inlet duct as an added precaution is however worthy of consideration

In its simplest form the plant for producing filtered air of low bacterial content consists of a fan drawing air through two suitable filters in series, followed by ultraviolet radiation in a short duct. The air could be adjusted to a suitable temperature by passing it through a standard electrical fan heater fitted with a thermostat

The problem of removing steam from the theatre can be dealt with by providing suitably placed ventilators fitted with the valves I have described. The positive pressure will ensure the removal of the steam

The use of extractor fans for this purpose as has been pointed out in your columns, is highly dangerous. The organisms drawn in from the hospital will be all the more dangerous because a high proportion of them will be resistant to penicillin and other antibiotics.[2]

I am sure that the large pharmaceutical manufacturers would be very willing to offer the wealth of their experience, through their medical information departments, to anyone requiring assistance in planning a suitable positive-pressure plant for an operating theatre

Southmead Hospital,
Bristol.
P J FOWLER
Chief pharmacist.

"YOUTHFUL CONTRIBUTORS"

SIR,—With humility and no little trepidation being still fairly young myself I write to question the need of older eminent writers to mention in the course of controversy in your columns, the age of their adversaries

Aspects of two subjects were recently raised about which it is surely generally accepted, there is still much to be known—namely the treatment of schizophrenia and the variability of intelligence I thought many of the points put by your correspondents were of help in getting a better understanding of the present knowledge of these subjects

It seemed therefore, to me, the more the pity that it was found *necessary* to criticise subjectively, on the grounds of their age those whose work stimulated useful discussion Surely the value of research and premise should be able to be judged objectively

Equally unfair would it be for the younger of us to draw attention to the age of your older contributors

St Clement's Hospital,
Ipswich.
M F BETHELL

DOSAGE OF MEPHENESIN

SIR,—In an earlier communication[3] I reported on the use of mephenesin in the treatment of various "rheumatic" complaints commonly encountered in general practice, and emphasised the importance of prescribing adequate dosage. The optimum daily dose, in my series of cases, was usually found to be 4–6 g given in divided doses every four hours, the minimum being two Tolserol tablets of 0·5 g four times daily Independently, Dr Nesbitt[4] has reported highly satisfactory results in 143 cases of similar disorders with associated spasm of skeletal muscle, and has suggested that tolserol should be given in doses of 1–3 g four or five times a day

Since my preliminary report was presented a number *of pharmaceutical firms have become interested in* mephenesin and I view with increasing concern the introduction of products containing the drug in quantities so minute that it can have no muscle relaxing effect Despite the wide differences between the doses which I have advocated and those provided by these products, the manufacturers concerned are quoting my report in their bibliographies.

My studies with this drug now include more than 400 cases, and I am convinced that it is very valuable for the treatment of "fibrositis" and allied disorders involving muscle spasm provided that proper dosage is employed. It should be stressed, however that any tendency to administer it in useless dosages will bring the drug into disrepute, thereby eventually causing sufferers to be denied a valuable adjunct in the treatment of "rheumatic" disorders

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[1] Sykes, G Carter D V British Pharmaceutical Conference, 1953.

[2] Rountree, P M Thomson E F *Lancet* 1952 ii, 6

[3] Pockover J R B *Ibid* 1953, i 1105

[4] Nesbitt, W R *Clin. Med.* 1953 60 289

Worthing J R B Peckover.

IDENTIFICATION OF PILLS

SIR,—The letter from Dr McQuitty in your issue of Dec 5 raises an important question Apart from exceptional circumstances, patients should know the medicines they are taking, because mystery and magic are unworthy of the physician who is a scientist and not a "medicine man" For this reason chemists should write the name of the medicine on the label of the container, or leave the original name on a container of a proprietary brand of medicine They should also return the prescriptions to the patients, who can thus follow more accurately the instructions of the physician—except, of course, in cases of dangerous drugs In Continental countries chemists are obliged to label the name of the medicines (even the formulæ of complex prescriptions) and to return the prescription This also helps to avoid accidents, which are far from rare

Changes of habit are imperative from this point of view Even Plato wrote in his *Laws* that the physician when dealing with free citizens must explain the medicines he prescribes, and only with barbaric slaves need he not take this trouble I am interested to note that Dr McQuitty got the chemist to put the name on the container by writing his instructions in Latin I have written similar instructions in English for years without any result—I shall try Latin next time

London W 1 A P Cawadias

METHYLCELLULOSE FOR OBESITY

SIR,—Like children who have been eating sweets before meals, obese overeaters who have been taking methylcellulose drinks beforehand cannot manage much either If they are instructed to be selective about what they leave—bread, potatoes, &c—they find their weight comes down after a while This, at any rate, was the experience of 10 people who tried the experiment

Of the ætiological factors in obesity, overeating from whatever cause is probably the commonest To cut down intake is easy enough in theory, but once overeating has become a habit or a "conditioned reflex," it is difficult, in practice, for the sufferer to eradicate it without help A number of remedies have been tried, with varying success, ranging from advice to dextro-amphetamine and minimal doses of sodium amylobarbitone, but the preparation I recommend is methylcellulose jelly, which has the advantage of being an indigestible bulk substance

A simple trial, lasting eight weeks, was made on 10 obese men and women whose overweight varied from 1½ to 4 stone They were otherwise fit and doing a normal day's work The results were good, including loss of weight of from 7 to 30 lb without any significant side-effects It was unusual to lose weight during the first week Some people experienced feelings of faintness or hunger occasionally, but a sweetened drink corrected this. Some were given vitamin capsules but those who did not have them are not showing signs of deficiency Furthermore, some of the group claim that on stopping methylcellulose jelly, they no longer have the desire to overeat—in effect a "reconditioning" to reasonable dietary habits appears to have taken place Only time will tell how long this effect will last, but once overeating recommences a return to the overweight state is inevitable As the trial was not strictly supervised and several people admitted forgetting their "dis-apéritif" on occasions the results are encouraging

Methylcellulose, a substance resembling "wood wool" swells up when suitably treated with water to form a 'jelly' It has been used as a bulk aperient in 22½ grain doses and his aspect is well described in Martindale, with a caution bout ossible formation of methyl alcohol in the intestine o reason, I prescribe only a week's supply at a s fear may be unfounded Mr K Gillanders

M.P S, kindly experimented to find a suitable form for di pensing This was found to be methylcellulose gr 7½ wit water to ½ fluid ounce (flavours as required, but it is left unflavoured) The method of preparation is important, however add to the required amount of methylcellu five times its weight of hot water, ensure that the mass thoroughly "wet," leave for about 30 minutes, make up volume with "chilled" water, and stir.

The patient adds a tablespoonful of the methylcellulose je to ½ pint of water (preferably) or other liquid In water it colourless and tasteless This is taken ½–1 hour befo meal times It is necessary to tell the patient that t mixture must be made up to ½ pint with liquid and th he must experiment as to the time of taking it He must n be discouraged if there is no loss of weight in the first wee The rationale of the treatment should be explained in simpl terms this is important, for an obese mentally defectiv patient (I Q 60), who was incapable of appreciating the rationale, gained 4½ lb during treatment.

The cost of ingredient for the jelly for 3 weeks' treatment is about 8*d.* wholesale, which compares favourabl with a proprietary preparation in tablet form (with vitamins) at 14*s* retail for the same period

Botleys Park Hospital,
Chertsey, Surrey J. N Badha

GRADING OF S.H M.O.s

SIR,—The whole profession is now aware of the wide spread 'dissatisfaction and feeling of frustration amon senior hospital medical officers in the Health Servic This letter is to present their case and to enlist sympath and active support in their efforts to secure justice

The arbitrary splitting of the ranks of specialists in two distinct grades was the mistake Gross injustice were done in the original grading, and indeed this wa recognised by the fact that subsequent reviews wer made These, however, have themselves been the subjec of criticism just as severe, and that there were stil prima facie instances of injustice was admitted in Dr Rowland Hill's annual report at the Cardiff meetin of the B M.A in July

Apparently no proper basis was ever laid down fo determination of grading Therefore, assessments in different areas have turned out to be contradicto This is well illustrated by the last and "final" revie when all the S H M O s who applied for upgrading in th North West Region were successful, yet, among tho who similarly applied in the North East Region, no one was made up to consultant rank. I believe o specialist who worked in both areas was upgraded the one and not in the other

There are three main groups of S.H M.O.s

(*a*) General practitioner specialists.
(*b*) Young specialists
(*c*) Older specialists

(*a*) A member of this group is generally satisfied with his lot He finds the interest of practising his specia a welcome change from general practice, and, as he not dependent on it financially, the question of salary not important Probably he is attached to a sma hospital and is on its staff committee, therefore h has reasonable control over the running of his department

(*b*) The young specialist who eagerly accepts the pos of S H M O as a stepping-stone to consultant rank finds on applying for a consultant post, that there are few such posts available and that he is faced with keen compe tion by registrars, perhaps from teaching ho who may well have excellent testimonials from e medical authorities As he fails to obtain one post another he tends to drift into the last group

(*c*) The position of the older S H M.O.s is indeed less under the present system What committe going to appoint a senior man at a higher salary f short term of service when a younger officer is availa with most of his professional life to come? Many of th S.H M O s have worked for years under the old system for no reward and now feel that they have had to accept a position of inferior professional standing Much despondency exists in the whole of this group and this must be reflected eventually in their work by a falling off in initiative and enthusiasm Their only hope of promotion lies in another ' national emergency '

Representation —Many S.H.M.O.s who are in complete clinical charge of their departments have no direct say as to how they should be run Whatever recommendations they have to make must be done through a third person

Remuneration —All S.H.M.O.s are agreed that the rate of pay compares very unfavourably with that of consultants, G.P clinical assistants, administrative medical officers and certain technicians.

A number of recognised consultant posts are filled by S.H.M.O.s, and their status and remuneration should be altered accordingly ' Consultant status and pay for consultant work.'

Lastly, and this point demonstrates the opinion of the Ministry of Health official secrecy surrounds the grade of S.H.M.O No list of names and addresses of officers holding this grade is allowed to be published.

Support is asked for either abolition of this grade and substitution of assistant physician, assistant surgeon &c, or for the following resolution

(1) That there should be an annual or biennial review of the grading of all S.H.M.O.s.

(2) That S.H.M.O.s should have full representation on committees controlling their work arrangements and other departmental interests.

(3) That the rate of remuneration should be revised

All can help by bringing this subject up for discussion publicly Such action would be welcome support for the negotiating committee of the B.M.A

G WARING ROBINSON
Chairman and Acting Secretary
S.H.M.O Group Leicester and Chairman,
Combined Groups, Sheffield Region.

Leicester

EHLERS-DANLOS SYNDROME AND SUBCUTANEOUS MOVABLE SPHERULES

SIR,—The Ehlers-Danlos syndrome is a developmental mesenchymal dysplasia, often of strikingly familial incidence (mendelian dominant) The complete form is distinguished by the association of three main gene-abnormalities of development (1) over-elasticity of skin; (2) over-extensibility of joints and (3) friability of the skin and its blood vessels This last feature leads to the broad transverse papyraceous scars, which, when present across the knees constitute an almost pathognomonic sign of this syndrome. The over elasticity of skin, often particularly evident in front of the chest tends to be associated with a certain amount of cutis laxa, especially about the elbows where there are not rarely loose connective tissue lumps, or so-called pseudo-tumours (sometimes termed the fourth sign of the syndrome)

But the purpose of this letter is to draw attention to a fifth and no less interesting feature of the condition —namely the occasional presence of small pea-sized spherules which are freely movable in the subcutaneous tissue under the most elastic portions of the skin. Their presence may be missed on a superficial examination, and indeed may not be detected by the patient himself They seem to be due to an abnormal arborescent " growth of lobules of subcutaneous fat, some of the lobules becoming constricted and dropping off into lymph spaces, communicating freely with one another Probably in time, the separated lobules may become minute, oil containing, cyst-like spherules, with thickened or even calcareous walls.[1] The free movability of the spherules signifies to my mind a peculiar dysplasic arrangement of subcutaneous lymph spaces, analogous to, and perhaps a minor form of the very rare condition of subcutaneous lymph sacs or cushions " first described, I believe by Kuultzky and Melchior[2]

London, N W 1 F PARKES WEBER.

MELAMINE RESIN IN THE MAKING OF PLASTER CASTS

SIR,—In 1951 at the American Medical Congress held in Washington a film was shown by Dr M Cobey illustrating the incorporation of a resin called Melmac in plaster casts Melmac is the trade name for the substance melamine formaldehyde On further inquiry it was found that this material was made by Lederle Laboratories, but at that time a sample could not be obtained However on returning to Britain it was possible to get a similar substance marketed under the name of Beetle Resin ' by British Industrial Plastics Ltd This costs 5s 3d per lb Since then the resin has been incorporated in many plaster casts made in our hospital, and, apart from some initial difficulty in finding the correct temperature at which to use it, no serious difficulties have been encountered. When resin is used with plaster-of paris a lighter, stronger plaster can be made, and this is of considerable advantage especially when treating children suffering from bone and joint tuberculosis If radiographs are required through the plaster cast the thinner cast obtained by using the resin results in better detail

I have been informed by British Industrial Plastics Ltd that only one other hospital in Britain has been supplied with resin for this purpose, the request for it, in May 1953 was made after a demonstration to one of their orthopædic surgeons in Belfast.

Very little has been written on this subject In America, Spittler et al[3] reported two years experience with melamine formaldehyde in the making of plaster casts. They studied the properties of such casts in detail and came to the conclusion that it is possible to produce a stronger cast of reduced weight and bulk which is more resistant to moisture and soiling than the ordinary plaster cast The only other literature on the subject which could be found was an article in *Modern Packaging*[4] in which a method is described of using fibre cans containing a 'Polythene' bag into which the plaster bandage is dipped after adding water and catalyst to the resin in the bag Each fibre can is discarded to avoid clogging of plumbing with the plaster resin mixture, but in practice here we have had no trouble with clogged drains.

The method used is as follows:

300 g of resin is weighed out and to this is added 30 g of ammonium chloride which acts as a catalyst and speeds setting The mixed powders are then added slowly to one litre of warm water mixing them in by hand. The temperature of the water should be about 130 F to start with, and a good working temperature after dissolving the powder is about 120 F In all about 4 litres of water may be required adding from time to time to the original solution while the cast is being made This is done to prevent the plaster which may fall off home-made bandages forming with the resin a solid mass in the basin. It is necessary to work rather more rapidly than when using plaster bandages and water alone for if one is slow and the temperature of the soaking fluid is allowed to fall then a thick plaster cream may form. This can however usually be dissolved by adding more water, but this procedure may dilute the resin too much When the cast has been made some of the cream in the basin can be used to give a smooth glazed and partially waterproof exterior

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[1] Parkes Weber F Aitken, J K. *Lancet* 1938 i, 198.

[2] *Arch. Derm. Syph. Wien*, 1916, 123, 133 See also Sheldon J H. *Proc. R. Soc. Med.* 1934 27 633; Atkinson, F R B Parkes Weber F *Brit J Derm.* 1938, 50, 207

[3] Spittler A W Brennan J J Payne J W *U.S. Forces med. J* 1953, 55, 373

[4] *Mod. Packag.* 1953 26, 90

Finally the bowl is washed out by adding a large volume of water and the solution is poured down a sluice

The setting of plaster is generally regarded as an alternating process of dissolution of soluble anhydrite or calcium sulphate hemihydrate, or both, and crystallisation of the dihydrate gypsum as a mass of interlocking crystals Colloids such as glue or gelatin increase the viscosity of the solution, retarding circulation or molecular mobility and interfering with crystal growth, thereby retarding setting Urea formaldehyde resin solutions tend to retard setting in a similar way On the other hand, salts which tend to increase the solubility of gypsum in water tend in small amounts to accelerate the rate of setting Ammonium chloride and hydrochloric acid have such an effect

Formaldehyde combines quantitatively with the ammonia of ammonium salts in general and liberates the acid Urea formaldehyde resins behave similarly, but more slowly, and the free acid then promotes further condensation of the resin, resulting in setting and hardening Setting of the plaster thus takes place in a medium of progressively increasing viscosity Possibly the net result with a urea resin plaster mixture is a finer grained cast comprising smaller crystals superficially glued together with urea resin and less dependent upon mechanical interlocking for ultimate strength

Spittler et al mention that 3 out of 7 children in their series developed dermatitis This has not occurred in any of our patients, but it is advisable for the operator to use gloves, for if the resin and ammonium chloride are mixed with the bare hand, the skin begins to tingle and redden

In applying the resin soaked plaster bandages, it is advisable to put them on, especially in the case of body casts, a little more tightly than usual, for on drying the plaster tends to spring out from the skin a little It is found that the casts set more rapidly than is usual and quickly become very hard. Removal of the casts is said to be more difficult because of their hardness, but we have found no particular difficulty in taking them off, using either a simple plaster knife, plaster shears, or an electric cutter In this hospital plaster casts are always finished off by coating them with celluloid dissolved in acetone to which calcium chloride has been added, and this procedure also strengthens the surface of the cast while making it waterproof and very easy to clean It has not, however interfered with the removal of the cast even when it ha been made with resin

NUMBER OF BANDAGES AND WEIGHT OF CAST, WITH AND WITHOUT RESIN

Age of patient (yr)	Part plastered	No of bandages				Weight of cast (lb)	Remarks
		8 in.	6 in	4 in.	2 in		
12	Leg	1	1	—	2	—	300 g resin
10	Double hip spica with extension to lt. ankle	2	4	—	3	$8\frac{1}{4}$	300 g resin
		5	5	—	1	—	200 g resin
5	Jacket with shoulder straps	—	3	—	1	—	300 g resin
		12	—	8	—	—	Without resin Patient now in this cast
3	Jacket and rt arm down to wrist	—	4	—	2	$2\frac{1}{2}$	300 g resin
4	Jacket only	—	5	1	—	—	150 g resin
17	Double hip spica with extension to lt ankle	6	6	—	—	$9\frac{1}{2}$	300 g resin Without resin, a similar plaster weighed 21 lb
12	Double hip spica with extension to lt. ankle	8	13	—	2	11	300 g resin
		11	8	13	4	14	No resin (Plaster cracked in upper part)

The accompanying table gives a few examples o comparative numbers of bandages required, and th weights of some casts made with and without resin The figures clearly illustrate the considerable saving i plaster bandages and the reduction in weight which ca be achieved by this method It is evident that 300 g resin is about the correct amount to use, for with 150–20 g more bandages are required If the solution is mad too concentrated and if the temperature is too high, the resin settles out as a sticky rubbery mass on the basin an on the operator's fingers as he mixes it In order t simplify matters, a firm making plaster bandages ha been asked to try and incorporate the resin into the plaster bandage, but so far they have been unable to d this

Abergele Sanatorium,
North Wales

JOHN B MORRISON
Medical superintendent.

FAIR PLAY FOR THE STAMMERER

SIR,—The rapid increase in the number of speech therapists has brought with it a correspondingly widened scope of activity, but there is a danger that the cases which should have priority will be pushed aside in favour of those that are easier to treat

As a former stammerer, like many of the pioneers of speech therapy, I decided to give up general teaching to devote all my time to the correction of stammering and cleft palate speech, but as soon as I accepted a post on the staff of a teaching hospital I found my clinic crowded out with backward speakers, lispers, &c, most of whom would correct themselves if left alone or who could be dealt with by a school-teacher or parent By seeing such cases once and once only I was able to concentrate on the stammerers

The stammerers should enjoy priority if only because the great majority are above the average mentally—indeed a considerable proportion are of scholar or exhibitioner standard—nor are they less able to take a lead in games They are, in fact, potentially valuable citizens handicapped only by a speech habit which has developed in the majority of cases by direct or indirect imitation After their correction by speech re education, stammerers are able to take their rightful positions in the world, but many are being held back in favour of children with ordinary baby inaccuracies and, even worse, of mentally deficient children

Within the last few months a very bright little boy of 10 was taken to one of the teaching hospitals, after waiting for very nearly two hours his mother was told by a student that there was a waiting-list of a year The speech therapist in charge had seen neither the mother nor the boy, nor had there been any examination or interview The mother wisely decided to seek private treatment and the stammer was corrected. Had that step not been taken the result might have been similar to another experience Several years ago a bright boy won a scholarship to one of the London grammar schools but when interviewed by the headmaster the boy was refused because he stammered he turned to mechanical work which he disliked, so after seven years he gave it up He now drives a taxi

The correction of typical infant speech disorders is straightforward and makes no great demands on the speech therapist, and it may be interesting to increase the vocabularies of the mentally deficient, but the former will correct themselves in most cases, while the mentally deficient can never become such useful citizens The correction of the stammerer's speech calls for endless patience, while the psychological repercussions that often develop make great demands on the personality of the teacher, but it is more than worth while because it enables the stammerer to assume his rightful position and the mmunity to benefit from his abilities Speech therapy a vocation and if treated so will secure for the mmerer the priority he deserves

H ST JOHN RUMSEY
Consulting speech therapist
to Guy's Hospital.

London, N W.1

THE INSULIN MYTH

Sir,—Dr Hunter's contribution (Nov 28) to the ntroversy over the respective merits of E C T and ep insulin in the treatment of schizophrenia is in ct an attack upon *all* physical methods of treatment. hile not being representative of the views generally ld in the department of psychological medicine at uy's Hospital on this subject—for which all honour the individuality of the author—it contains a certain mount of special pleading The clinical improvement isplayed by patients who respond to deep insulin erapy is not a mere induced anosognosia; nor is ch treatment simply an irrational therapy

Apart from the work of Quastel Himwich and ellhorn, mentioned by Professor Mayer Gross in his tter in the same issue there is a recent paper by Lovett oust[1] which describes the effects of insulin-coma erapy upon blood-oxygen saturation, emphasising he correlation between a significant increase in such vel following treatment, and clinical improvement n the patients so treated—The author points out that is investigation confirms essentially similar findings y other workers of the effects of insulin therapy upon rterial pressure and cerebral metabolism

Deep insulin treatment remains in fact a standard rocedure for selected cases of schizophrenia treated n the York Clinic of this hospital where it seems to ost of us to continue to be justified by results

Guy's Hospital,
London, S E.1

DAVID STAFFORD CLARK

CORTISONE AND RHEUMATOID ARTHRITIS

Sir,—It was a pleasure to read the article by Dr West nd Dr Newns in your issue of Nov 28 The statement hat cortisone acetate (50–75 mg daily) administered to 27 patients with rheumatoid arthritis over an average period of nineteen months was not to be recommended nd does not favourably influence the course of rheumatoid disease, is of considerable importance especially coming from rheumatologists. The conclusions were reached in a controlled series with a very fair assessment, based on accepted criteria

As they point out, the profound effect of cortisone in a daily dose of 100 mg or more on the symptoms and signs of the disease in the early weeks of treatment is an acknowledged fact but doses of 75 mg or more can rarely be maintained for many months without serious complications

Since its introduction into this country from the U S.A , the supplies of cortisone have depended on dollar exchange or generous gifts, and the restricted amounts, more precious than gold have been delegated to various hospitals and centres for treatment of rheumatic diseases where fundamental or essential research was supposed to be carried out, although much of this had already been adequately completed on a vastly larger scale in America.

Although it is accepted that cortisone in addition may be of considerable benefit in some of the collagen diseases certain skin diseases eye conditions, and acute rheumatic fever the more rationally and logically treated diseases such as Sheehan's syndrome, Addison's disease and adrenocortical hyperplasia with excessive androgen production, have had to manage with second best or merely glean the crumbs which dropped from the rich man's table Other indications are already apparent from the literature such as cortisone maintenance following hypophysectomy or bilateral adrenalectomy for advanced carcinoma of breast or prostate or for gross hypertension

It is very laudable that we should gain experience with this new hormone and confirm or confute the American experimental work but it was estimated last year[1] that home production of cortisone would exceed the then consumption by July of this year I understand that much of the material hitherto in use in this country was made by the French laboratories of Roussel, whether or not the dollar exchange operates here, I do not know Further, I am informed that in the not too distant future, more manufacturing chemists will be making cortisone in Britain

May I make a plea that cortisone should be more readily available to the medical profession and not only to the privileged few I feel that there are already adequate safeguards in the N H S both in hospital and general practice to deal with unjustified use of expensive drugs, and, as regards the dangers of overdosage it is reasonable to assume that if a doctor is sufficiently intelligent to prescribe the correct dose of morphia insulin nitrogen mustard or a host of other more potentially harmful substances then he is fit to treat his patient with cortisone provided there are acknowledged indications.

Most new therapeutic discoveries suffer at first from over-enthusiastic use and wild claims, but in the end a reasonable and balanced judgment prevails, and Dr West and Dr Newns must be congratulated on helping to swing the pendulum

Bristol.

GEORGE L. FOSS

FLORENCE NIGHTINGALE HOUSE

Sir—Advanced work for nurses was an important aspect of Florence Nightingale's nursing policy She wanted nurses of all nations to be what she called missionaries of health ' by training others and raising the standard of health wherever they went

Next year will see the centenary of Florence Nightingale's mission to the Crimea The National Florence Nightingale Memorial Committee in the United Kingdom is seeking funds to establish permanently a fitting memorial to her noble work and inspiration It is proposed

(1) To endow a residence for 44 nurses of all nations while undergoing advanced courses in London

(2) To further the advance of nursing education by the award of scholarships.

Throughout the world, similar national committees are raising funds for the award of scholarships to nurses They are all part of the Florence Nightingale International Foundation which is concerned with nursing education internationally

The successful candidates come to Britain and reside at Florence Nightingale House 173–175 Cromwell Road S W.5 during their postgraduate training adding an additional responsibility to the committee in this country but this is the land of Miss Nightingale's birth and we must not fail in our duty to her memory

We therefore appeal to everyone who appreciates her magnificent work for the nursing profession and to everyone who has experienced the kindness of a nurse, and to everyone who wishes to express in tangible form their gratitude Please either send a donation, or write for a copy of an informative illustrated booklet to the Florence Nightingale Memorial Committee of Great Britain and Northern Ireland, 12, Whitehall, London, S W 1

LUKE
Chairman.

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[1] Doust, J W L. *Canad. med Ass. J* 1953, 69 108.

[1] See *Lancet*, 1952 ii, 992.

Medicine and the Law

Successful Appeal against Verdict of Negligence

EARLIER this year a patient obtained the substantial award of £4000 as damages in an action alleging the professional negligence of an anæsthetist[1] Admitted to Charing Cross Hospital for an operation for removal of the bladder, he received blood-transfusion, his left arm being extended for this purpose at an angle of 80° He complained that he subsequently suffered a loss of power in the arm amounting to paralysis The verdict has now been set aside by the Court of Appeal[2]

The evidence of medical practice was clearly the crux of the case, and the argument and judgments on appeal have made it clear that the trial judge was impressed by the fact that, when the operation occurred in July, 1950, the defendant doctor was unaware of an article published in *The Lancet* in the previous January[3] The judge evidently took the view that a failure to keep abreast of the professional journals was negligence The Court of Appeal is satisfied that, if the negligence amounted to no more than this, it is not enough. There was evidence at the trial that abduction up to 90° would do no harm Statistics showed, said Lord Justice Somervell, that in only approximately one-third of 1% of such operations did brachial palsy follow, and generally it was not permanent The learned Lord Justice declared that there was no evidence of negligence Concurring with this opinion, Lord Justice Denning commented that actions against hospitals were now becoming common It must be understood, he said, that not every mishap which might occur in the course of hospital treatment would place upon the hospital the burden of an explanation Mishaps often occurred without negligence on anyone's part The plaintiff had entered the hospital for an operation to save his life It had been proved that the hospital exercised all reasonable care As for the *Lancet* article, "it would be putting much oo high a burden on medical men to say that they must ead every article in the medical press."

Alleged Negligent Certification

In a recent action[4] at Hampshire assizes the plaintiff, a State registered nurse and the proprietor of a Bournemouth nursing home, claimed damages for having been, as she alleged, wrongfully certified as a mental patient and put into a mental hospital Her counsel, opening her case, said that in 1949, when she was 43, she had suffered from a septic condition of the finger nails, perhaps due to overwork, undernourishment, and possibly mental strain In November she entered the defendant doctor's nursing-home for rest and treatment By Nov 23 he reached the conclusion that she required to be certified, she was sent to a mental hospital

Giving judgment for the defendant, Mr Justice Parker said that the plaintiff's description of conditions in the mental hospital had been exaggerated and false, though not deliberately so She had felt herself persecuted by members of the medical profession and in particular by the defendant. His Lordship was satisfied that she really was mentally ill when she went to the defendant's nursing home The defendant had consulted a specialist, and this precaution completely exonerated him from any charge of having failed to exercise reasonable care in taking the step of certifying the patient The court, however, allowed the defence only 50% of the costs because of certain difficulties placed in the plaintiff's way, the absence of records, and the consequent

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1 See *Lancet* 1953 1 906
2 *Times* Dec. 8
3. *Lancet* 1950 1, 99 103
Manchester Guardian, Dec 2 and 9

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protraction of the proceedings The judge said h that the medical defence society concerned mig it was a case in which they need not ask even 50% allowed

Obituary

WILFRED SHAW

M A., M D Camb, F R.C.S., F R.C O G

Mr Wilfred Shaw, surgeon in charge of the gyn logical and obstetrical department at St Bartholome Hospital, died in London on Dec. 9 a few days befo his 56th birthday By his death his specialty has l an original mind and a fine surgeon, and his hospi one of her most distinguished sons and loyabl characters

He was born in Birmingham, the son of the late Isaac Shaw, J P, and educated at King Edward's Scho Birmingham, and St. John's College, Cambridge, whe he was open scholar, foundation scholar and exhibitio and Wright's prizeman, and took a first-class in par in the natural sciences tripos. He consolidated t successful start by winning at Barts the Matth Duncan prize and gold medal, the Lawrence rese scholarship and gold medal, and the Cattlin resea scholarship Thus early he showed the bent inquiry to which we owe his classical papers on ov tumours and the anatomy of prolapse.

He qualified in 1921, took the F R.C.S. in 1923, an proceeded to the M.D in 1928 During these years served a useful apprenticeship at Barts as midwif intern and, later, as house-surgeon to Sir Charles Gordon Watson and as chief assistant for two years to the dep ment of obstetrics and gynæcology But not con with these postgraduate qualifications, he sought fur experience in Vienna. The Viennese school was influence him for the rest of his life, for there he learn to master the technique of vaginal surgery

In 1926, the post was created at Barts of residen assistant physician accoucheur, which was at that unique in London. This post carried with it consider teaching responsibilities and the handling of a l number of obstetric and gynæcological emergenc Wilfred Shaw was the inevitable first choice for appointment, which he held continuously for five yea and from which he acquired a solid clinical experien second to none in the country In 1931 his postgradua studies were rewarded with the Jacksonian prize of th Royal College of Surgeons, and in 1933 an Arno demonstratorship followed—both rare distinctions for a gynæcologist. In 1932 he was elected F.R.C.O G

He was elected to the honorary staff of Barts in 1931 as assistant physician accoucheur His new appointment gave him full scope to develop his gifts as clinician and teacher. As a teacher he was superb, and his lectures and grinds were the ultimate basis of that world-famous book, Shaw's *Textbook of Gynæcology*. He always ma tained that this book was inspired by, and intended fo his own Barts students In a few pages it certain contained enough meat to pass all the exams, not exclud ing the M.R C O G As an examiner in the Conjoint London, and Cambridge finals, he was scrupulously and generous to a fault, as many an unhappy candida will bear witness. He disliked examining because kind heart and sensitive nature rebelled against inflictin a penalty on a student whose ability he instinctivel divined, however poor his showing under the fire his co-examiner At examiners' meetings he was a fearl champion of the doubtful candidate, and this somet led him into conflict with his colleagues.

J H. writes: "Wilfred Shaw was more than gynæcologist, he was an anatomist, a scientific sopher, and probably the greatest gynæcological p logist in Britain. The Williamson Laboratory at was dear to his heart, and here, with his old and technician Bert Cambridge, he cut, stained and examined many thousands of sections, and his colle of slides and specimens is testimony to their ti industry He had a great reputation as a patholo and his colleagues and friends from all would bring him difficult slides for his interpretation and judgment. He always had a microscope in outpatients and in his consulting-rooms, and after a cursory glance, he would resolve the problem with a curt diagnosis. There was no court of appeal and, if there was, the old man was almost invariably right. Incidentally, he christened himself the ‘old man’ with that puckish self depreciation which at first perplexed but ultimately endeared him to us all

‘His housemen and students learned to await with lively anticipation his invariably punctual arrival in the Rolls—never driven over forty in its life—the gay salutation, the teasing repartee the teaching round packed with wit and wisdom.

“His teaching sessions in outpatients were unforgettable. Though his students came to learn gynæcology, they achieved more than this simple object. Elizabethan poetry and drama, higher mathematics, nuclear physics, international politics the history of Barts, all came within the syllabus. He knew the name of every Barts student, his history, his wife’s name and the number and names of their children, whom he had probably delivered himself His amazing memory was once tested on View Day, when Barts is at home to all her old students. A quiet, unassuming middle-aged general practitioner approached Wilfred to pay his respects with the remark You won't remember me Sir I haven’t seen you for twenty years. A puzzled frown gave place to sudden enlightenment as he saluted his old student by name and inquired after his wife and partner Shaw was a voracious reader and reviewer of the British and foreign literature, and his memory seemed to enable him to place his finger on any article about any subject and to quote the author almost verbatim.

‘Wilfred loved people To him his patients were all real friends and he knew all about them and their families. His old outpatients adored him and his private patients invariably became his friends. No service, great or small was too much trouble to him and he lavished his care upon them for small or no remuneration He had an enormous practice amongst doctors wives, and his great house in Harley Street was choked with the tokens of their gratitude Here he would receive a visiting Indian surgeon an old Barts nurse, a student in need of advice a young aspiring consultant, or a gynæcologist with a difficult slide; each with a problem for this good Samaritan and beloved physician, to the solution of which he bent his rich wisdom and kindness.

“As a surgeon, he was quick, dexterous and neat, essentially an anatomical operator, he invariably found the correct plane of cleavage His repertoire of operations was limitless but he was at his best with a difficult vaginal procedure say a tricky vesicovaginal fistula. All prolapse surgery, and, in particular, the problem of stress incontinence and hernia of the pouch of Douglas, is the richer and better for the anatomical researches and the carefully planned techniques of Wilfred Shaw He loved the skill and artistry of operative technique and he chose to spend his last two years writing the textbook of gynæcological surgery which he finished a few weeks ago When this book is published, it will stand as a monument to his courage as a man and his greatness as a surgeon.

‘Si fractus illabatur orbis
Impavidum ferient ruinae.

Mr Shaw leaves a widow, three sons, and a daughter

Appointments

South-Western Regional Hospital Board:

[illegible], SALVINO M.D. D.Sc. Malta, D.OBST.: registrar in obstetrics and gynæcology Bath group of hospitals.

[illegible] C. D R. M.B. Brist. M.R.C.P.E. senior medical registrar West Cornwall clinical area.

RICHARD D R., B.M. Oxfd surgical registrar Weston-super-Mare General Hospital.

[illegible], E. J., M.B. Capetown surgical registrar Cheltenham General Hospital.

The Hospital for Sick Children, Great Ormond Street, London:

[illegible], JOAN M.B. Glasg., M.R.C.P.: house-physician.

CALDER, ANNE, M.B. Edin., F.R.C.S. house-surgeon.

FERGUSON ALEXANDER, M.B. N.Z. F.R.C.S.: house-surgeon.

THOMSON M. F., M.B. Glasg.: asst. resident M.O. Tadworth.

WALLMAN L. S., M.B. Adelaide, M.R.A.C.P.: house-physician.

Notes and News

MEDICAL RESEARCH COUNCIL OF IRELAND

THE many investigations sponsored by the Medical Research Council of Ireland during 1952 are described in some detail in the annual report that has lately been published. The work on the chemotherapy of tuberculosis has continued with renewed vigour, thanks both to the enthusiasm of Mr Vincent Barry D.Sc., and his colleagues and to the generosity of University College Dublin, in providing the first instalment of a grant from the Lasdon Foundation The grant made it possible to carry out extensions to the council’s laboratories. An interesting observation made during the year’s experiments was that isoniazid resistant strains of tubercle bacilli show a greatly reduced virulence for guineapigs.[1] A number of novel derivatives of isoniazid have been synthesised in the laboratories; some of them show activity of the same order as isoniazid but further inquiries are needed to decide whether any of them are significantly better than isoniazid

Among other investigations, Dr T Counihan has made phonocardiographic studies of presystolic triple rhythm and the opening snap of the mitral valve Evidence from œsophageal phonocardiograms suggests that there are two auricular sounds, the first probably produced in the auricle itself and the second in the ventricle as the result of auricular action The latter sound is normally inaudible, but it becomes audible in heart-block, constituting then a form of presystolic triple rhythm. Dr Counihan has been working on this subject at the Postgraduate Medical School of London.

Prof W J E. Jessop has conducted a survey by means of a simple screening test for disturbances of carbohydrate metabolism of a diabetic type among elderly patients attending a urological clinic. The results showed that about 25% of patients over the age of 60 had a metabolic disturbance of diabetic type Many of them did not require treatment but in some cases insulin was necessary As yet it is not possible to say how far treatment of the metabolic disorder affected the course of the disease for which the patient came to hospital in the first place

During the year the council spent £8678 on general research and £8942 on work on the chemotherapy of tuberculosis. Other expenditure included £600 on cortisone research and £17 346 from the special grant for the National Tuberculosis Survey

TEETHING-POWDERS

LAST week (p 1247) we discussed the use of teething powders, and we are glad to record that Messrs. John Steedman & Co makers of a popular powder have announced that they had decided some months ago to remove calomel from their powders. Distribution of the new mercury free powders began this month. This wise decision was made public on Dec. 9 at an inquest[2] on a 10 month old girl who had died of pink disease.

DANGEROUS DRUGS ACT

AN order[3] which came into operation on Dec 14 applies part III of the Dangerous Drugs Act, 1951 to the salts of N Allylnormorphine and any preparation, admixture extract, or other substance containing any proportion of N Allylnormorphine which will as from Dec. 14 come within the provisions of the Dangerous Drugs Act and the regulations made thereunder

SOCIAL SECURITY BENEFITS

RECIPROCAL arrangements on social security benefits between Great Britain and Australia will come into force on Jan 7[4] The arrangements will enable people who go from this country to Australia to receive benefits under the Australian scheme to supplement any retirement pension or widows benefits which they may be receiving from the Ministry of Pensions and National Insurance People who come from Australia to this country will be treated as if they had been insured under the National Insurance schemes while they were in Australia so as to help them to qualify for National Insurance benefits here

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1 Barry V C., Conalty M. L Gaffney E. *Lancet*, 1953, i, 978
2 *Times*, Dec 10 1953
3 The Dangerous Drugs Act, 1951 (Application) (no. 3), Order 1953 S.I 1953 no 1680 H.M. Stationery Office 3d
4 The National Insurance (Reciprocal Agreement with Australia) Order 1953 S.I. 1953 no. 1772. H.M. Stationery Office. 6d.

A separate agreement with Australia on family allowances will come into effect on the same day under regulations which are being made by the Minister of Pensions and National Insurance This will ensure that families going from one country to the other will be able to qualify for family allowances in the new country as soon as they arrive there

MEDICAL ARCHIVES

A DOCTOR'S diary giving details of George III's illness, diaries of a surgeon who sailed in emigrant ships to Australia (1840–50), and a licence to practise medicine (1777) found among a collection of papers in Dorset are among the items of medical interest in the latest *Bulletin* of the National Register of Archives. The official correspondence of Sir Stafford Northcote, 1850–55, now calendared by the register, includes letters from Florence Nightingale The most important manuscripts in the collection of the Royal College of Physicians of London are also listed in the *Bulletin*, they include deeds from different parts of the country, ranging from 1444 to the present century

The National Register of Archives was set up in 1945, under the Historical Manuscripts Commission, and its purpose is to collate, and as far as possible to collect notes of the contents of, ancient and modern documents in private hands, or belonging to local authorities and institutions such as hospitals, and societies. The address of the register is c/o the Public Record Office, Chancery Lane, London, W C 2 The National Register of Archives for Scotland is at Register House, Edinburgh

FILMS ABOUT MOSQUITOES

THE Wellcome film unit has produced two new 16-mm films, *The Dissection of a Mosquito for Malaria Parasites* and *Pinning Mosquitoes* Both are in colour with sound.

The first is a demonstration by Mr P. G Shute, of the Medical Research Council's Malaria Reference Laboratory The phases of the life cycle of the malaria parasite within the mosquito are briefly described and the appearance of both oöcysts and sporozoites is shown. The film then demonstrates how the salivary glands of the insect are pressed out and prepared for examination so that the sporozoites can be identified. The removal of the stomach and the detection of oöcysts are then demonstrated The running-time is 10 minutes.

The second film shows how mosquitoes should be pinned, how to stage and label the pinned insects for permanent display, and how to pack them for dispatch through the post It was produced in collaboration with the department of entomology at the London School of Hygiene and Tropical Medicine The running-time is 5½ minutes

The films may be borrowed on application to the public relations officer, Burroughs Wellcome & Co, 183–193, Euston Road London, N W 1

JEWELLERY AS THERAPEUTIC OCCUPATION

ABOUT five years ago the Goldsmiths' Company[1] pointed out that simple jewellery and metal work would be a satisfactory form of occupational therapy for many patients obliged to spend a long time in hospital Having gained the support of the appropriate organisations, it gave a grant to Mr Claude Geoffroy Dechaume, a designer craftsman, enabling him to demonstrate to occupational therapists the possibilities and limitations of such work, and under the company's auspices he produced a book on *Simple Craft Jewellery*,[2] soon to appear in a second edition. Based on this book a film of the same name has now been made by Mr F H. Dowden of the Ministry of Education, and it had its first showing at Goldsmiths Hall on Dec 7 to representatives of the Association of Occupational Therapists, the British Red Cross Society, the Central Council for the Care of Cripples, and other bodies concerned with the teaching of the disabled Intended for use in hospital occupational therapy departments, training schools, craft workshops, and the like, the film shows how patients doing this work. A small but fascinating exhibition of various kinds of jewellery, mostly made with inexpensive materials, was on view at the hall during the subsequent few days, for the benefit chiefly of students of occupational therapy It can hardly have failed to make them emulous

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[1] *Lancet* 1948 ii 315

[2] See *ibid* 1949 ii 1010

Royal College of Surgeons of England

At a meeting of the council on Dec 10, with Sir Reg Watson-Jones, vice president, in the chair, Dr Fred Rankin, president of the American College of Surgeons, awarded an honorary fellowship. Hunterian professor were awarded to Mr R C Evans and Dr Michael W for a lecture on the Ascent of Mount Everest. The Re prize was presented to Margaret M. Heley (Royal Free

Diplomas of fellowship were granted to the following:

J A. James, K. L. Barnes, C M Phillips, R B McGrigor, D Moffat, R. M. Harvey G F Hird, J S J Morley, J E Ol L G Fison, Kenneth Till, A S Falconer, A E Flatt, R A Da J A. G Holt, Betty M L. Underhill, Julian Bihari, P. B. Kor Sankar Panikkar, B G Reynolds, Agnes R. D Bartels, J Snyder, K. S E MacRae, Margery Scott-Young, C J S Se Mohamed Shafi, G C. Pritchard, K. G Malcomson, J McE I M. Grant, H D W Powell, Fouad Hussein Gamali, J D Glanvil Wilfrid Grundill, P A P. Joseph, Ali Masood Akram, Alexand Benjamin, R. F. Burton, J K. Craig, W S. Foulds, Ped Kra Ghadiali, Braham Goldman, R. J Hart, K. W Hinrichsen, Godf Sorabjee Karai, J S. Lekias, Elaine Lister, E. A. McVerry, K D Vowles, Khalid Hassanein Abdel-Ghaffar, Arun Kumar Das, Iv Sober, J B R. Wells, C G Wilson, W S. Wilson, F J Hall, H Jones, John Kiely, B V Kyle, E D. McIntyre, S A Mell D J Retief, J E S Scott, N J Way, R F Zacharin, A F G Anderson, R. R. Barnett, J G Brice, A F Ferguson, H. R. McC Mithlesh Kumar Mehra, A G. Morgan P J Mortensen, G Smedley, T K. Thorlakson, Martin Wynyard, John Chalme David Davies, L R. De Jode, E S P Ferguson, Rambir Sa Gupta, O H Maclaurin, Barry Shandling, Katyayani Kuma Sinha.

Royal College of Physicians of Ireland

On Dec 4 the following, having passed the final examina of the conjoint board of Ireland, were admitted licentiate medicine and midwifery

A. M. van Bergen, Constance M. Coogan B C. F. Dalton, J Devlin, G G Dibue, Eileen M. Dodd, Kathleen M N Gilmo T S. Gilpin, Milton Jeffries, Wee Soon Lee D M. McCarthy, R McKenna, Monica M. McLoughlin, Priscilla R. K. Nicol, Am Nwogu Obonna, Abdul Rasoul Ghulam Hussein Peermoham N B Smyth, E H. Wells, R J Whitty, W J. Wilmot, Mitch Wright, Maria E T Wyganowska

Conjoint Board in Ireland

At recent examinations for postgraduate diplomas th following were successful

D C.H —N Adhya, Muriel Bannister, Margaret Bell, Ros Power

D.A —R. E. Bourke, P J Boyle, Una B Byrne J G Goodbo Mary M Gordon, R. C Gray, J Levin, J Lomax, L. C Lu R. W Milner, D O'Leary, E F O'Riordan, M. R. Porter,

Royal Faculty of Physicians and Surgeons of Glasgo

At a meeting of the faculty on Dec 7, with Dr Andr Allison, the president, in the chair, the following were admitted fellows of faculty

Saw Mra Aung H. W Boyd, Thomas Cochrane, A Tuboku Metzger (qua physician), J P Fraser, Shimoga Rangam navara Ganeshiya (qua surgeon)

General Nursing Council for Scotland

Dr W A Murray, superintendent of East Fortuna Sa torium, has been appointed a member of this council. Pr G Wishart, Dr A D Briggs, Dr W G Clark, and Dr Ma Esslemont have been reappointed.

British Association of Otolaryngologists

The following Officers have been elected for 1953-54 president, Mr V E Negus, immediate past-president Mr H V Forster, vice-president, Mr I. Simson Hall, hon secretary, Mr Myles L Formby hon. treasurer, Mr W Mill

General Practice on Sheffield Housing Estates

Sheffield Corporation has refused to provide sites f doctors to build their own houses and surgeries on housin estates, because it believes that permanent surgeries would prejudice the creation of health centres. The corporation hopes to establish an experimental health centre on the new estate now being built at Greenhill, but is willing i the meantime, to provide doctors who wish to practise on th estate with houses or flats on a short-term lease, say of years

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The award of the first gold medal under the newly Sydney Body Trust has been made to Dr William Evans work in cardiology

The British Standards Institution has issued a standa (B.S 2044 1953) covering laboratory tests for resistivity conductive and anti-static rubbers. Copies (price 2s 6d.) may b obtained from the sales branch of the institution London, W 1

EDUCATION FOR ELIZABETHANS *

Lord RADCLIFFE
P C, G B.E., M A Oxfd
A LORD OF APPEAL IN ORDINARY

AT the recent congress on medical education much as said about the need for the future doctor to have general education and a general background of culture That is not a problem peculiar to those who are being ducated in the study of medicine You will equally nd today that those who are interested in, let us say he technical training of engineers advocate the advan ages of supporting their specialised knowledge with wider general education You will find that leaders f industry are begging that they should be supplied ith a stream of persons not merely qualified to be experts n their particular branch of study but also with a wider eneral background It is one of the problems of our ime. But what to do about it and how to solve it?

You see the times have changed since the days when eneral education represented a recognised curriculum t is quite right for the young person to wish to be a pecialist. If his wits are alive he realises as he advances n study the fascinations and the potentialities of his articular subject, and he dives rightly head foremost nto it with all the enthusiasm that he can command. It is a good thing for to become a master of a craft is something which gives a man self-confidence and a footing in life which he will not otherwise acquire. It is a good thing

Remember, too, that the days when there could be a man of universal knowledge have passed. The sheer accumulation of vast stores of learning in each field, the great range of subjects which are now open to be included among the various branches of learning have put us a century perhaps two centuries, beyond the time when any one man could say I represent universal knowledge and I see it all in all its branches under my eye, and I take a picture of the whole.'

Somebody once said that Sir Christopher Wren was one of the last of those universal men Others have claimed it for Goethe But if it were possible in those days, it is not possible now and with this enormous accumulation of specialised learning it has come about that the old general curriculum upon which education and culture were founded has broken up The mould is broken and there is not that set course of the humanities in which we were taught to believe in the past Indeed we are now called upon to remember that the old general classical education in the humanities was in its *day nothing but a vocational training to equip* candidates for the medieval Civil Service

But, again what is to be done? We all agree that we should be better men and fuller men if we had behind us a wider range of education. I am sure Twenty Questions on the B B C. however assiduously attended will not provide the answer nor even the illuminations of the Brains Trust nor even however well chosen a course of lectures on potted culture But if I may, I will make two suggestions to you which may be of some assistance.

* * *

One is to keep your curiosity alive. I should like to put in a word for the value of curiosity as one of the great influences of civilisation For it will come to pass, as you become a master of your own craft that the certainties recede, enthusiasms to some extent fade but if you can keep your curiosity and your inquiring mind alive, that you will find, will sustain you until the end. If I may say so, back your fancy; let your curiosity take you into the paths which fascinate you or appeal to you and do not let it be dominated by what other people around you or in the past have said are the great or the important or the beautiful things. If you remain curious and do not take things for granted you will find however specialised your path, that life is continually opening out before you and showing you new fields in which your mind can dwell

It is taking things for granted and not asking why and how they are there—the very denial of the scientific spirit—that makes people limited in their interests. We all look every day at the skyline of London and never ask ourselves by what miracle of energy and acquired skill that great monument of St Paul's still dominates the skyline of the City one of the great architectural monuments of the world. When we go to the country we look at the country scene and we never even notice, because it is so much there, that wherever we look there is a church spire which is part of the landscape We do not set ourselves wondering by what miracle of a continuity of civilisation we have come to take it for granted that the church spire is an inevitable part of every country scene

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In some countries, without a long history on record, it might not mean much to say 'Keep your curiosity alive,' because it might not lead very far, but in this country in which we are so intimately tied up, whichever way we move, with our own past history and the great civilisation to which we belong and have belonged it almost requires going about in blinkers not to be reminded of it.

Last summer at Stratford, I was struck by the evidence of the extreme popularity of Shakespeare's plays in this country today: crowds of people thronged the theatre at every performance, standing outside in queues for the chance of admission from a returned ticket for one of the five plays presented at the Festival I see that the Old Vic are presenting two more—perhaps one of the great Hamlets of our time—and are setting out on a cycle of five years in which they will produce in due order every single play written by Shakespeare a dramatist 350 years back from our times and of whose life and personality it would be true to say we know almost nothing

I was wondering whether this great feeling of response to Shakespeare's work today represents something that is common between the situation of our time and the situation of those times in which he wrote.

What piece of work is a man! he makes *Hamlet* say How noble in reason! how infinite in faculties! in action how like an angel! in apprehension how like a god! the beauty of the world! the paragon of animals!' So may we say as, with all the resources of modern civilisation at our command we realise the unlimited possibilities that stretch before the human creature—if only he will do himself justice.

Yet Shakespeare makes Hamlet place this creature with all his potentialities against a dark background:

> this brave o'erhanging firmament, this majestical roof fretted with golden fire why it appeareth nothing to me but a foul and pestilent congregation of vapours.'

So it may seem to us when we see the inmost secrets of Nature and the great resources that lie still untapped in the firmament conscripted to form the major instruments of man's destruction That seems to be the dilemma of our time, and I think it was felt the dilemma of the times of the first Elizabethans

Do we at all share their solution when we face our problems? They were a race strange to us for all our love of their literature. They were greedy and avaricious, they were ambitious, they had a mania for power, but they were men who had a taste for magnificence, they had a taste for greatness, and they had a feeling for what they understood by Honour By our standard they were curiously indifferent to success What mattered to them was the glory of the attempt and the achievement and not the ultimate reward or recognition

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* Part of the inaugural address given at Westminster Medical School on Oct 12, 1953 The full text appears in the Dec. 18 issue of the school magazine *Broadway*

You see it reflected so clearly in Shakespeare's plays Ie wrote comedies, of course—lovely fairylight things oathed in an unreal sunshine, in which nobody was supposed to take seriously what happened or the result "It is just the prettiest thing in the world," Lord Melbourne told Queen Victoria about *As You Like It.* But what Shakespeare never wrote, as far as I can remember, was a play in which the good man, while faced with adversity and tried by troubles, emerges triumphant and successful at the end What he wrote were these tragedies in which the great man—Brutus, Antony, Hamlet, Othello, Lear, Coriolanus—goes down to ruin, and goes down to ruin with those he loves involved in his destruction, not because of any challenge that he in his pride had made to fate, not because of any vice which is being punished or avenged by the moral law in his person, but because he is in the hand of a fate that is hostile to him and by a darkness that he cannot overcome

That is not a cynical or a desperate presentation of man's dilemma, because you do not feel while you watch these plays, nor do you come away at the close feeling, that darkness in the end is triumphant But they do throw you back to the feeling that it is not success or failure itself which is the thing for which man is set here in his environment, but that what matters is his total gesture, and that there are moments of great light in the life of every person—moments to which all of us, without reason and without philosophy, respond—which justify the human experiment At the end, I think, you feel vividly that although the solution may be hid in mystery, at least it is plain that the answer is not now and the solution is not here That is something of what the predicament meant to the Elizabethans

* * *

You may follow them further, if you care, in the works f the man whose tercentenary we were celebrating last ear—in Hakluyt's account of the Elizabethan sailors You will find a proud record of people of endurance and of daring who in little ships, of 20, 30, 50, or 100 tons, went out into the unknown Atlantic searching for the North-West Passage or out to the North of Scandinavia looking for the North-East passage—men who faced odds of all kinds without self pity and without complaint, against powerful enemies and more powerful fleets, against ice and fog and storm, against pestilence and disease, and men who at the same time had—or many of them had—a simple faith that they were in the hands of Providence in the risks that they were taking As one of them wrote in Hakluyt,

'God, who doth give limits to man's times, and ordaineth the manner and circumstance of dying"

But feeling themselves in the hands of Providence, they felt no less the need that they should show themselves skilful captains and skilful sailors, and when the end came, as it often did, in disaster and not in success, and one more ship and its crew went down in battle or the storm, they closed the record with dignity and without amentation This is what Raleigh wrote of his friend ir Richard Grenville after the ship *Revenge* had sunk ollowing the fight with the Spanish fleet

"What became of his body whether it were buried in the se on the land, we know not, the comfort that rem his friends is, that he hath ended his life ho respect of the reputation won to his nation and country, and of the same to his posterity, and being dead, he hath not outlived his own honour

Those are fine words.

I do not think it out of place to recall the na of those men, something of what they did and someth of what they believed, in this beginning of your term Coronation year, when we are told that we are to be second Elizabethans and there is a second Queen Elizabe on the throne It can not be wrong to recall that man of those men were citizens of this very ancient city which you do your work and that it was upon the Tham almost under these windows, that "they hoist up and committed themselves to the sea," just as t and the future years will bear you to your fu which will be, as I so much hope, happy and fru and not without adventure

INVESTIGATION OF OBLITERATIVE ARTERIAL DISEASE OF THE LOWER LIMB

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THERE is no general agreement about the value o various tests used to determine the integrity of peripheral circulation, and special investigations often considered to be of limited practical significance The widening of the field of direct surgical appro to diseased arteries has emphasised the importance an accurate knowledge of disordered function a anatomy We therefore felt the need to comp various methods of investigation and to assess th value, with particular reference to accurate diagno and treatment, and to ascertain which of these metho may usefully be retained in everyday practice O conclusions are based on a study of more than 100 patients with arterial disease of the lower limbs, althoug it was impossible to make all the investigations on each patient

Aims of Investigation

Before any investigations can be discussed, their aim must be clearly defined, and in the case of peripheral vascular disease these are as follows

(1) To establish, confirm, and amplify diagnosis.

(2) To distinguish between functional and organic arterial disease

(3) In the presence of organic disease, to obtain a p knowledge of *a*, the site and extent of any arterial block *b*, the condition of the arterial walls above and below the bloc *c*, the number, size, and position of collateral vessels, *d*, the patency and function of the arterial tree beyond the bloc with particular reference to the potential blood supply of th skin and muscles.

(4) To plan treatment

(5) To aid prognosis

Methods of Investigation

Arterial Pulsation

The Pachon oscillometer was used at mid thi mid calf levels and above the ankle

Skin Blood-flow

The response of skin-temperature to indirect-h was measured by the method of Lewis and Pick (1931) Skin temperature readings of the big toe, made on a Cambridge thermocouple skin thermom

Venous-occlusion plethysmography of the foot was done by the method of Barcroft and Edholm (1943)

Fluorescein-circulation rate was determined by the method of McGregor and Wayne (1951) and Goodwin and Kaplan (1951)

Calf-muscle Blood-flow

Venous-occlusion plethysmography was done before and after two minutes' exercise taken under conditions of temporary arterial occlusion.

Arteriography

This was done by percutaneous injection of 50% Diodone into the femoral artery at the groin, followed by serial radiography of the whole limb The details of the radiological technique have been described elsewhere (Jones and Steiner 1949)

All the investigations were made in the laboratory at a room temperature of 19·0–23·5°C.

ARTERIOGRAPHY

Although it is our object to assess the value of our methods in the light of our aims of investigation, if these methods are also to be compared and contrasted some common basis of comparison must be agreed on, In our opinion the only satisfactory basis for this purpose is an anatomical one Of the methods we used arteriography is the only one which enabled an anatomical analysis to be made of the disease process in the arteries of the legs we studied In view of this we used it as a standard by which to compare and contrast our other methods of investigation We relied on a pictorial rather than a quantitative assessment of arteriography, and the standards by which we assessed the arteriograms (fig 1) have been as follows:

(1) *The presence of disease shown by atheroma or by thrombosis.*

(2) *The collateral circulation, judged by the number size, and tortuosity of the collateral vessels and the filling of the distal arterial tree.*—A *good* collateral circulation was inferred from rapid filling of the main arteries beyond the block, through a satisfactory number of collateral vessels. A *fair* collateral circulation was inferred from delayed filling of the main arteries beyond the block through a few collateral channels. A *bad* collateral circulation was inferred from patchy filling or non filling of the main arteries beyond the block through very few collateral channels.

(3) *The circulation of the foot judged by the patency or absence of the dorsalis pedis and plantar arteries.*—We have accepted filling of both the dorsalis pedis and plantar arterial arches as indicating a good blood-supply to the foot, provided the collateral circulation round any proximal blocks was good When there was only partial filling of the plantar and dorsalis pedis arteries, the foot circulation was assessed as fair particularly if blocks were also present in the tibial and/or the peroneal arteries When the plantar vessels failed to fill the circulation was considered to be bad. In this connection it must be remembered that the dorsalis pedis artery is absent in about 8% of normal persons (Allen et al. 1940) Early venous filling on arteriography was accepted as evidence of a good collateral circulation and of a good blood-supply to the foot.

TABLE I—RELATIONSHIP BETWEEN AVERAGE OSCILLOMETRIC (PACHON) DEFLECTIONS AND ARTERIAL PATENCY DEMONSTRATED ARTERIOGRAPHICALLY

Level of application of oscillometer to limb	Major arterial thromboses absent	Thrombosis in femoral or popliteal artery		
		Tibial and peroneal arteries patent	One or more major distal thromboses	Total
Mid-calf	5	1·1	1·1	1·1
Ankle	2	0·6	0·6	0·6

Figures represent average oscillometric deflections.

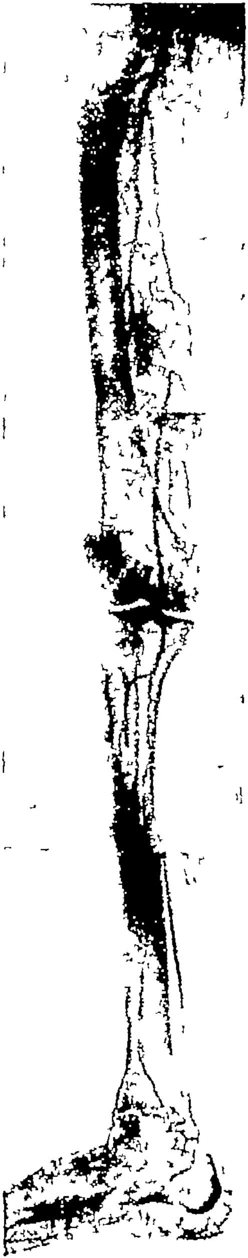


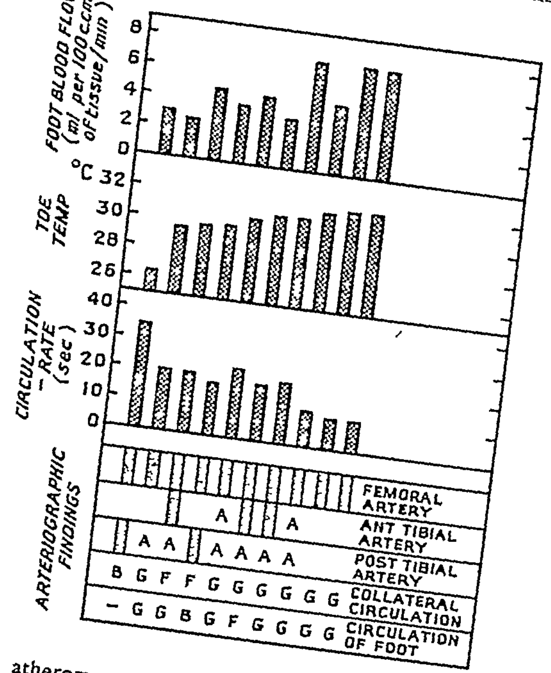
Fig. 1—Arteriogram of right leg in a man, aged 31 showing thrombosis of superficial femoral artery good collateral circulation, patency of distal arteries and good circulation in foot.

OSCILLOMETRY

A comparison has been made between the anatomical distribution of distal arterial thromboses beyond a femoral or popliteal block and the average oscillometric readings at mid-calf and ankle level in the same series of patients (table I) It is apparent that the presence of filling or obstruction of the tibial and peroneal arteries does not influence the average oscillometric readings in such circumstances

We have found that there is no constant relationship between the resting foot and calf flows and the oscillometric readings at mid-calf and ankle levels. This confirms the findings of Edholm et al. (1951) who showed that oscillometric readings measured by a cuff method give no indication of blood flow because the force of arterial pulsation may be inadequate to overcome the cuff pressure

Oscillometry is therefore of use only in diagnosing the level of the block, and of least value in assessing the collateral supply and patency of the main arteries beyond the block Early disease of the arteries before the occurrence of thrombosis is not demonstrated Localisation is not accurate enough to be of use for arterial grafting or for thrombectomy nor is the decision for or against lumbar sympathectomy influenced by the oscillometric findings, because these give no indication of skin flow Oscillometry has only limited value in deciding the level of amputation



A, atheroma present. B, bad F, fair G, good
Stippled columns, thrombosis

Fig 2—Foot blood-flow, toe-temperature, circulation rate and arteriographic findings in 10 cases of femoral artery thrombosis. Arranged in ascending order of toe-temperatures

FLUORESCEIN CIRCULATION RATE

This test was made, after indirect heating, by the method of McGregor and Wayne (1951) and Goodwin and Kaplan (1951)

In the presence of a femoral artery block, shown by arteriography, there was reasonably good correlation between the circulation-rate, on the one hand, and toe temperatures after indirect heating and foot blood flow measured by plethysmography on the other (fig 2) Limbs with a femoral block and good collateral circulation tended to have a short circulation time and high toe temperatures, but the converse was not necessarily true When all cases were considered together, only fair correlation was found between circulation rates, on the one hand, and foot blood flows and toe temperatures on the other (fig 3)

Measurement of the circulation rate, even when a substance with an objective end point is used, is not a particularly sensitive indicator of peripheral blood flow When the disease mainly involves the digital vessels, toe temperature recordings may not correlate with the circulation rate, which has been measured only as far as the dorsum of the foot Moreover we have found digital gangrene in the presence of palpable ankle pulses and good foot blood flow, in such cases it is not surprising to find the circulation rate normal The correlation between toe temperatures and circulation-rates in 10 limbs with femoral artery block (fig 2) is similar to that found by Goodwin and Kaplan (1951)—agreement between temperature readings for the skin of the calf and toes and fluorescein circulation times in 12 patients, most of whom had major arterial blocks. Th resence of normal skin temperatures an l finding in patients with organic se. ted by Pickering (1933), and

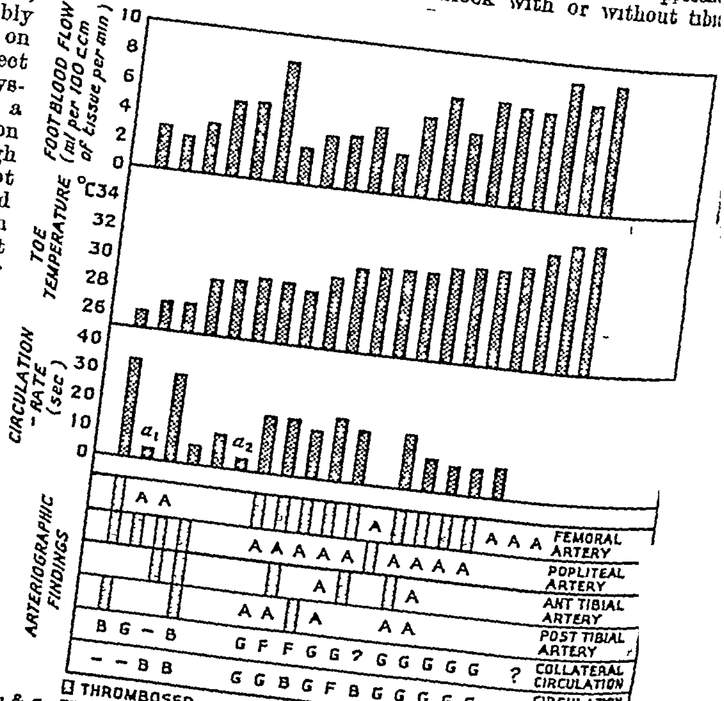
McGregor and Wayne (1951) occasionally noted normal fluorescein-times in such patients

FOOT PLETHYSMOGRAPHY AND TOE-TEMPERATURE RECORDINGS

Since little information can be obtained by examination under resting conditions, vasoconstrictor tone must be released before the efficiency of the circulation of the lower limbs can be studied Pickering (1933) showed that the temperature of an affected limb at rest may be increased above that of its relatively normal fellow Furthermore, recording of normal blood-flow does not indicate that the tissues are receiving an adequate bloc supply, because there may be deviation through arteriol venous anastomoses, the blood supply never reaching th capillaries (Abramson 1944)

We have obtained indirect vasodilatation of the lowe limb by the method of Lewis and Pickering (1931) We have measured the degree of vasomotor release obtained by recording the increase in the foot blood flow and in the temperature of the dorsum of the great toe, using an air filled venous occlusion plethysmograph and the Cambridge thermocouple thermometer

The relationship between foot blood flow after indirect vasodilatation and the anatomical lesion shown by arteriography is shown in table II 42 limbs were analysed, and the foot blood flows are presented in the table as an average for each group of anatomical lesions. Where thrombosis (but not necessarily disease) is absent, the average maximal foot blood flow measured 9 ml per 100 c cm of tissue per minute With a femoral or popliteal thrombosis but patency of all the major distal arteries, the average maximal blood flow was 5 2 ml The presence of an additional block in one or more of the tibial arteries led to a further reduction in the average maximal foot blood-flow to 3 9 ml If the last two groups are considered together—i e , in the presen of a femoral or popliteal block with or without tibi



□ THROMBOSED A, ATHEROMA PRESENT B, BAD F, FAIR G GOOD
a1 & a2 FROM SAME PATIENT IN WHOM FULL DILATATION DID NOT TAKE PLACE

Fig 3—Foot blood flow toe-temperature circulation-rate and arteriographic findings in 20 cases of obliterative arterial disease of the lower limb (all types). Arranged in ascending order of toe-temperatures.

TABLE II—FOOT BLOOD FLOW AND TOE TEMPERATURE AFTER INDIRECT HEATING IN RELATION TO ANATOMICAL FINDINGS BY ARTERIOGRAPHY

Anatomical sites of arterial thromboses shown by arteriography	Foot blood flow after indirect heating (ml per c.cm. of tissue per min.)		Average maximal toe temperature after indirect heating (°C) (normal = 33°C or more)
	Average maximum for each group	Range of maximum over each group	
All major vessels patent	9·0	5·1–13·5	32·0
Femoral or popliteal with or without tibial	4·0	2·5–7·2	31·0
Femoral or popliteal only	5·2		
Femoral or popliteal with one or more tibial	3·0		
Femoral or popliteal with one or more tibial and either or both plantar and dorsalis pedis	3·3	2·3–5·0	28·5
Tibial with or without either or both plantar and dorsalis pedis	5·5	2·8–8·5	32·0
Tibial only	5·5		
Tibial and plantar and/or dorsalis pedis	5·4		
Dorsalis pedis and/or plantar only	7·5		

thrombosis—the average maximal foot blood flow was 4·0 ml. In the presence of superadded thrombosis of the dorsalis pedis and/or the plantar arteries the foot blood flow was further reduced to 3·3 ml. Where the thrombosis was confined to the tibial and peroneal arteries the average foot blood flow was 5·5 ml. and the presence or absence of additional blocks in the main arteries of the foot did not seem materially to affect blood flow in the foot.

The average toe temperature for each group is also recorded in table II. In our experience the average toe-temperature reached in normal people after vasodilatation has been 33–34°C. It will be seen that a difference of only 1°C was recorded between the average maximal toe temperatures in normal limbs and in those limbs in which atheroma but no actual thrombosis was present. A similar difference was found between the latter group and limbs with femoral artery thrombosis without additional blocks. It is only when there were additional blocks beyond the femoral and popliteal arteries that there was a significant drop of 2–5°C in the toe-temperature after the indirect heating. Toe temperatures are thus less helpful in diagnosis than are measurements of foot blood flow; but, if a major block of the femoral or popliteal artery is present, a failure of the toe temperature to reach 30°C after indirect heating strongly suggests the presence of additional distal blocks.

It must be emphasised that these figures are averages, and there is a wide range between the maximum and minimum in each group, presumably owing to variations in the anatomical lesion, the collateral supply, the degree of vasomotor release, &c. It is therefore impossible to discover the degree of ischæmia present in the foot by measurement of the foot blood flow after indirect vasodilatation, and only when the sites of the main arterial blocks are known is it possible to interpret the foot blood flow as above or below the average for that group of patients. In our experience these measurements do not necessarily bear any relation to digital gangrene which may be established even though the peripheral pulses may be palpable and the foot blood flow within the normal range.

The relationship between foot blood flow and the anatomical lesion shown by arteriography clearly indicates that the foot blood flow may be approximately assessed from the arteriogram.

As has been mentioned, we have compared circulation rates, toe temperatures, and foot blood flows, and fig. 2 shows that, although a correlation between these tests is evident in limbs with a femoral-artery thrombosis, the correlation is less convincing when all the cases are considered together (fig. 3).

The direct comparison between foot blood flows and toe temperatures (fig. 4) shows that correlation is fair when all types of cases are considered and good in cases having femoral artery blocks only.

Return of vasomotor tone after sympathectomy was first noticed by Lewis and Landis (1930) and Lynn and Barcroft (1950) showed that the resting blood flow in the foot had returned to within twice the preoperative level within seven days. From our own experience, and from a study of their paper it is apparent that no relation exists between the preoperative maximal foot blood flow after indirect vasodilatation and the ultimate resting foot blood flow after lumbar sympathectomy. It is therefore difficult to gain by preoperative tests anything but an impression of the results to be expected after sympathectomy. The nearest approach to accuracy is that a patient should show clinical improvement. Because a direct approach to the vessel is still of limited application, surgery has little to offer these patients other than sympathectomy as a prophylaxis against gangrene, and in our experience preoperative investigation seldom influences the decision for or against this operation. In general, it can be said that a good clinical assessment is sufficient for other than academic purposes.

CALF PLETHYSMOGRAPHY AFTER EXERCISE

Resting calf blood flows are of no significance in the accurate assessment of the potential blood-supply to the muscles of the calf, the measurement of which has always presented difficulty. Various methods have been used: for example, Boyd et al. (1949) use a claudicometer designed to measure the onset of claudication at a controlled speed of walking over measured distances. Various forms of ergometer have been devised (Shepherd 1950, Simmonds 1936, Hitzrot et al. 1936).

We have used the venous occlusion plethysmograph filled with water at 34°C to measure the calf blood flow

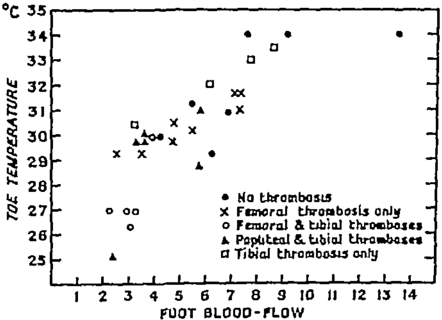
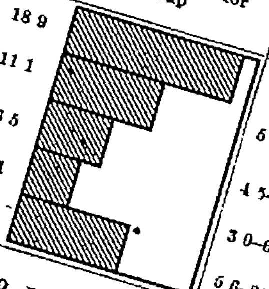


Fig. 4—Correlation of foot blood-flow and toe-temperature after indirect heating (30 limbs).

TABLE III—CALF BLOOD FLOW AFTER EXERCISE IN RELATION TO ANATOMICAL FINDINGS BY ARTERIOGRAPHY



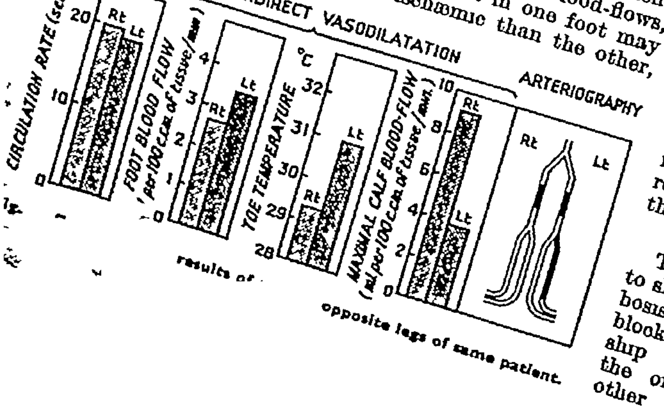
Anatomical sites of arterial thromboses shown by arteriography	Calf blood flow after exercise (ml per c.cm of tissue per min) Average maximum for each group	Range of maximum over each group	Return of calf blood-flow to within 1 ml. of resting range (min.)
All major vessels patent	18·9	9·0–26·0	5·0
Femoral only	11·1	6·3–19·0	7·5
Femoral and tibial	6·5	4·5–11·5	6·5
Popliteal and tibial	5·1	3·0–6·7	5·2
Tibial only	11·9	5·6–22·0	4·0

before and after two minutes of graduated exercise taken under conditions of temporary arterial occlusion.

In the analysis and interpretation of the results obtained from this test three variables have to be considered (1) the maximal blood-flow obtained, (2) the time required after exercise to reach this peak 'blood flow—vasodilatation in muscle is already full at the end of a period of arterial occlusion (Lewis and Grant 1925), and (3) the time taken for the calf blood-flow to return to within the resting range. In table III the anatomical site of the arterial lesion shown arteriographically is compared with the maximal calf blood-flow obtained after exercise. The highest average flow of 18·9 ml per 100 c cm of tissue per minute was obtained when thrombosis in the major arteries, but not necessarily disease, was absent. With femoral arterial thrombosis alone the average peak calf blood flow was 11·1 ml, and, when the lesion was peripheral to the popliteal bifurcation only, the average peak blood-flow was 11·9 ml. The combination of femoral and peripheral thrombosis reduced the average maximal calf blood flow to 6·5 ml, and in those limbs in which peripheral arterial blocks were associated with a popliteal thrombosis 5·1 ml, the lowest reading in all the groups, was recorded. This is not surprising, because it is in these cases that the origin of the sural arteries is most often involved in the disease.

The range between the highest and the lowest maximal calf blood flows in each group is also recorded. As with foot blood flows after vasodilatation, this range is wide, particularly where there are no blocks, or when the block is limited to femoral or peripheral arteries alone.

This pattern is similar to that followed by foot blood flows after vasodilatation, but we have been unable to find any definite relationship between these and the maximal calf blood-flows obtained after exercise. Indeed, in comparing contralateral limbs in the same patient (fig 5) we have found that, whereas foot blood-flows, toe temperatures, and circulation-rates in one foot may suggest that limb to be more ischæmic than the other,



results of

opposite legs of same patient.

the calf blood-flows after exercise have indicat reverse. In this case the arteriographic finding with the calf blood-flows, and we believe that blood flow after exercise is a better index of the circulation of a limb than are methods invo measurement of vasodilatation in the foot.

The delay in reaching maximal calf blood-flo exercise is found only with femoral or higher, and may well be of artificial origin. Neverthel practice it has been found that the longer the dela less efficient is the collateral circulation.

It has been shown by Grant (1937) that, after an rapid return towards the resting blood flow, the blood-flow after exercise may remain at a level 1 ml per 100 c cm of tissue per minute of the resting blood-flow for as long as twenty minutes have confirmed this, and in our analysis of calf blood flows after exercise it has been thought advisable accept a return to within 1 ml. of the previous blood-flow as the point of return to normal. In table these figures have been arranged for each group of but the only significant fact that emerges is is a longer delay in femoral arterial blocks either or without additional peripheral blocks than in or tibial blocks.

Conclusions

It is clear from our attempts to compare these of investigation that in obliterative arterial disease,

TABLE IV—ASSESSMENT OF VALUE OF TESTS USED INVESTIGATING PERIPHERAL VASCULAR DISEASE OF LOWER LIMB

	Diagnosis and assessment of circulation						Influence on choice of treatment		
	Level and extent of block	Collateral system	Condition of arterial walls	Patency of main peripheral arteries beyond block	Potential skin blood flow	Potential muscle blood flow	Lumbar sympathectomy	Grafting, &c.	Level of amputation
Clinical history and examination	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes
Oscillometer (Pachon)	Yes	No	No	No	No	No	No	No	Yes
Tests measuring vasodilatation									
Toe-temperature	No	Yes	No	Yes	Yes	No	No	No	No
Circulation rate	No	Yes	No	Yes	Yes	No	No	No	No
Foot plethysmography	No	Yes	No	Yes	Yes	No	No	No	No
Calf plethysmography after exercise	No	Yes	No	No	No	Yes	No	No	No
Arteriography	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes

Yes of value No of no value.

two limbs are alike, the variety of anatomical lesions infinite and the overlay of vasomotor control never th same. We have shown that a quantitative control is limited in its application unless exact anatomical correlation tions are known. Bearing this in mind, we have marised (table IV) the value of the tests we have sum regards the aims of the investigation which we stated the outset.

OSCILLOMETRY

This is of no help in clinical assessment other than to show the upper limit of the level of an arterial throm bosis. Assessment of prevailing conditions below the block is impossible, because there is no constant relation ship between arterial patency and blood-flow, on the one hand, and oscillometric deflections, on the other

Comparisons can only be made between contralateral mbs in the same patient, and not between one patient nd another

As regards treatment, oscillometry is perhaps of mited value in assessing the level of amputation

TESTS OF VASOMOTOR RELEASE

oe-temperature Foot Plethysmography and Fluorescein rculation Rate

The measurement of toe temperatures has proved to e the best method of assessing an individual digit ut may bear no relationship to proximal conditions of rterial competency and any correlation between the wo can only be applied in its widest sense.

Foot blood flows provide the best assessment of the lood-supply to the foot, and a definite relationship etween this and the anatomical lesion has been shown The correlation between foot blood flows and toe emperatures is approximate, and is greatest in femoral hrombosis uncomplicated by distal blocks.

We consider that the fluorescein-circulation rate is slightly inferior test to toe temperature recordings, xcept when a femoral block is present, in which case igh skin temperatures and a short circulation rate uggest a good collateral blood supply The circulation ate is of no value in determining the presence or absence of a thrombosis in a major vessel.

It therefore follows that the interpretation of these methods as a quantitative method of investigation s only acceptable if the exact anatomical lesions are nown, and even then the technical limitations of the tests must be taken into account

As regards clinical assessment no information is obtained about the level of the block and early disease s not discovered, assessment of the collateral system and patency of the arterial tree is indirect and limited n application

It is our opinion that tests of release of vasomotor one, though important for physiological research, are of little clinical value in the accurate assessment of pathological conditions. As regards treatment, we do not consider that the results of these tests influence the decision for or against any form of surgical operation

Calf Plethysmography

Although this gives a better idea of total blood supply to the limb than do tests of vasodilatation it is of little clinical value and certainly of no value as a guide to treatment. Direct correlation cannot be made between calf and foot blood flows.

ARTERIOGRAPHY

This is the only method which allows an accurate assessment of the presence of early disease, the level and length of the block, the condition of the arterial wall and patency beyond the block The collateral supply cannot be quantitatively estimated but a study of the number calibre and tortuosity of the vessels gives valuable information The skin blood flow may be judged approximately and a relationship of the origin of muscular vessels to the site of disease is of significance (fig 1)

As regards treatment, arteriography is of little value in the selection of patients for sympathectomy but essential if direct arterial surgery is contemplated. It is very useful in decisions about the level of amputation

Arteriography should not be used as a routine but reserved for (1) confirmation of early organic disease (2) cases in which direct surgical intervention on the artery is a possibility, and (3) a preliminary to amputation in certain patients.

From a practical point of view it cannot be too strongly emphasised that a careful analysis of the clinical history and examination will provide as adequate a guide to treatment as, if not a better one than, any method of special investigation (except when direct surgical intervention on the artery is contemplated) If additional information is required arteriography is the method of choice

In the investigation of peripheral vascular disease it is a common habit to focus attention as we have done here, on an attempt to assess disturbances of function As we have shown little information is gained which is of value in selecting the type of treatment required Further work will be necessary to correlate these diagnostic tests with the results of treatment and thus to assess their value in this connection.

We are grateful to Dr O G Edholm for his help and advice

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REFLECTIONS ON DIABETES MELLITUS

ANSWERS TO A QUESTIONARY

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Musing upon the literature of diabetes mellitus recently I was struck by much conflicting evidence Whittaker (1949) writing on the handling of diabetic children condemns the notion that insulin treatment with free" diet will give adequate control, pointing out that children treated in this way are ill grown and undernourished, alternating between hyperglycæmia with symptoms and severe insulin reactions. Goadby (1950) found evidence in a carefully observed series of 43 patients, that unrestricted carbohydrate diet with insulin did not harm the patients and tended to reduce ketonuria. Goadby and Jacobs (1950) as a result of a pilot survey have propounded a hypothesis as follows

> (1) The control of diabetes mellitus as practised in the light of present knowledge, is without effect on the incidence of the long term complications of hypertension retinal and lens changes, and vascular disease
>
> (2) The control of diabetes does influence the incidence of neuropathy
>
> (3) In controlling the sugar metabolism we are not treating the underlying pathological condition which causes both the metabolic defect and the vascular and eye changes which may accompany it.

Jackson et al. (1950) believe that in children, a high level of control is not only possible but is the best form of preventing or delaying chronic degenerative changes. Root et al (1950) think that poor control and the duration and severity of the disease all play a part in promoting the onset of degenerative processes in diabetes and that it is impossible to apportion the blame with any accuracy Hunt (1951) in an impressive paper based upon vast personal experience pours scorn upon any kind of dietetic regimen for a diabetic, except one who is too fat On the other hand Wilson et al (1951a) believe that dietetic control is more important than any other known factor, such as duration or severity, in preventing degenerative vascular complications, and Spoont et al (1951) produced evidence showing that poorly controlled diabetics are more prone to retinopathy than well controlled patients, but they shrewdly point out that the evaluation of the degree of diabetic control is difficult

Wilson et al (1951b) give a good working classification of what they understand by "excellent," "good," "fair," and "poor" control, and they believe that any guidance falling short of good control permits diabetic nephropathy They describe 37 patients, in a series of 247, who maintained excellent or good control for a long time and escaped nephropathy Beaser (1951), in a survey similar to that of Wilson et al, found a similar response in a larger group of patients Wilson et al (1951c) compared two groups of young diabetics one group was controlled by a careful adherence to diet and normoglycæmia, the other was on a "free" diet with sufficient insulin to ensure health despite steady hyperglycæmia The first group was less susceptible to complications than the second, but by no means exempt

Among the other evidence, Zubrod et al (1951) believe that the onset of Kimmelstiel Wilson lesions coincides with a change in the character of diabetes of such a degree that progressively less insulin may be needed Hall (1952) thinks that glomerulosclerosis is one manifestation of a generalised vascular degeneration in diabetic patients and that duration and poor control both promote this process Lawrence (1952) has formulated rules, arising from his very great experience, for the guidance of diabetics who drive vehicles upon the roads Keiding et al (1952) believe, as a result of really substantial work, that good control of diabetes is more important than any other factor in the prevention of complications Hinkle and Wolf (1952) in an admirable survey bring out well the importance of stress and strain, as compared with relaxation and security, in the assessment, fluctuations, and day-to-day management of diabetics

With all this in mind I sent a questionary to 142 physicians, like myself, in charge of diabetic clinics, asking them a number of simple looking questions, and this is the result

The Questionary

The questionary itself brought the following response

Prompt replies	66
Delayed replies	15
Regret inability to help	6
Curt refusals	2
No replies	53
	142

Most of the replies were generously informative, often running into many sheets of closely written manuscript

I thus found myself with 81 reports on the modern handling of diabetes mellitus in clinics up and down the country, and the results can be condensed thus

Question (*a*) —Replies to preliminary questions showed that about 75% of all patients attending our clinics use insulin.

Care and Accuracy of Patients

Question (*b*) —What proportion of your patients taking insulin satisfy you that they are careful and accurate ?

All	6
Most	45
Probably about two thirds of them	11
Less than half	6
Difficult to assess	13
	81

Two physicians wrote

"The m[illegible]y of patients measure the insulin correctly but do [illegible] diet restrictions at all accurately, nor are they particularly careful in the care of their syringes and needles."

"I think probably 75–80% are accurate and careful, but I have to be very searching in questioning them Periodically I find that owing to the different strengths, patients are taking half or double the number of units I believe them to be taking In these cases if the follow up tests are satisfactory I simply discuss how many marks on the syringe they should take"

Hyperglycæmia or Normoglycæmia ?

Question (*c*) —Do you believe in mild hyperglycæmic control or normoglycæmic control ?

Normoglycæmia (including 2 emphatically)	26
Mild hyperglycæmia (including 2 emphatically)	38
Does not believe normoglycæmic control possible	1
We aim at normoglycæmia but usually have to be satisfied with mild hyperglycæmia	11
It depends on individual needs	4
Indecisive reply	1
	81

The answers included the following

"We prefer our diabetics who are taking insulin to pass a little sugar in their water, and are satisfied as long as their blood sugars are below about 200 mg per 100 ml and *there is no ketonuria*"

"The answer is 'it all depends upon the patient' Naturally I like them to be as near normoglycæmic as possible, but in many of the severe cases we have to be content with mild hyperglycæmic control so as to avoid hypoglycæmic reactions"

"I believe emphatically in normoglycæmic control, and am equally strongly against mild hyperglycæmic control, unless there is some good reason for it, such as a low renal threshold."

Carbohydrate Consumption

Question (*d*) —If you prescribe a diet, how many grammes of carbohydrate do you think adequate for a man of 140 lb ?

Between 200 and 300	16
About 200	20
About 150	9
Between 150 and 200	10
Depends on his work	20
About 120	2
No diet is prescribed	3
Not applicable (children's clinic)	1
	81

Some of the points made in replies were

"Where insulin is taken the diet is approximately 200 g of carbohydrate daily Non insulin takers are given 100 g a day as a minimum"

"Elaborate calculations are not used Not less than 160 g —but the final decision is based on appetite, type of work, and weight"

"We prescribe diets here in calories rather than in grammes of carbohydrate, but our 2500 calorie diet, which is the one most frequently used, contains 280 g of carbohydrate"

"In prescribing amounts of carbohydrate, I am guided, on the whole, not by consideration of how much carbohydrate a man of a given weight should take, but more on whether the patient is under or overweight If significantly over weight then the patient is placed on a reducing diet, usually containing from 100 to 140 g of carbohydrate If underweight, or of average weight, then in a great majority of cases carbohydrate is prescribed according to his wishes, the dose of insulin, if necessary, being adjusted. Himsworth's work some years ago would suggest that, in people of normal weight, diet should contain at least 200 g of carbohydrate as lesser amounts tend to alter their insulin sensitivity"

Adherence to Diet

Question (*e*) —What proportion of your patients taking a diet satisfy you that they adhere to it reasonably well ?

All or nearly all	4
The great majority	37
About half	22
The minority	5
Very few	7
Not applicable	1
Unanswered	5
	81

The following statements represent the views expressed:

Of the mild obese diabetics, approximately 50% adhere satisfactorily to the diet. Of the others a considerable proportion only diet sufficiently to relieve symptoms.'

The majority of patients on insulin adhere to the diet reasonably well. If they do not ketosis and pre-coma betray their backsliding but this is unusual The obese patient, whom I always attempt to control without insulin, is a more difficult problem, although once having lost weight the improvement in their sense of well being and appearance will impress on them that diet restriction is worth while '

It is almost impossible to say how many patients really do adhere to their diet. I feel it is probably only a small proportion who keep strictly to it, but gross excesses are rare, except in the cases of those who are on a 1000-calorie reducing diet and yet continue to gain weight.

" Almost all patients lie as regards keeping their diet."

"The great majority I am sure take a steady diet. The English man and woman are very conservative and once they get into a routine with no sugar or sweet food I don t think they alter much except on specific occasions, such as weddings when they generally ask for advice before There are of course some—especially young people and children—who run away with sweets and puddings, but on the whole if they have enough to eat and are not hungry, I don t think they do so'

Complications

Question (*f*)—Do you think there is any connection between hyperglycæmia and the complications of diabetes such as retinitis, cataract, gangrene nephritis and phthisis?

Comprehensive yes	30
Comprehensive no	6
Don't know	18
Unanswered	3
Yes, but unsure of the evidence	6
Yes, but uncertain about phthisis	9
Yes but uncertain about cataract	2
Yes, but uncertain about nephritis	5
These maladies appear to be independent of the degree of control imposed	2
	81

The answers included these remarks

There is no doubt that there are some elderly conscientious and intelligent patients who develop these complications irrespective of their diabetic control I am beginning to think that nephritis is commoner in the long standing diabetic who has not been ideally stabilised.'

"Yes: though it is my experience that in gangrene the body weight is more important—i.e., fat patients are more likely to get gangrene

I am quite sure a tight normoglycæmic control is essential in patients with phthisis and those patients presenting with retinitis, cataract gangrene and nephritis are usually those who have been inadequately controlled in the past. I believe that hyperglycæmia should be prevented if possible

"I am absolutely certain there is no connection between hyperglycæmia and retinitis, cataracts, and nephritis. There is an undoubted connection between hyperglycæmia and gangrene phthisis, and neuritis.

I cannot convince myself that there is a real connection between hyperglycæmia and the diabetic arteriosclerotic complications. Phthisis I do think is more liable to occur in an uncontrolled diabetic than in a normal young person

Strictness of Diet

Question (*g*)—Do you teach strict dietetic regimen or do you condone a certain laxity in a prescribed diet or do you allow a completely free diet regulated by insulin?

Strict dietetic regimen is taught	37
Laxity in a prescribed diet is condoned	27
Free diet regulated by insulin is our plan in many cases	3
We teach strict diet in young people and allow laxity in other patients	8
My policy varies with each patient	4
There is no such thing as a "free" diet	2
	81

Here again much diversity was evident:

"Patients are certainly taught strict dietary régime with carbohydrate intake balanced against regular insulin.'

"I teach strict dietetic regimen and allow no laxity I certainly do not teach a strict dietetic regimen I do however, insist that no sugar or sweet food should be taken because I think that it is absorbed into the blood so quickly that it upsets the balance I try to adapt the diet to the patient s ordinary meals and general way of life."

"We do not teach a strict dietetic regimen, except in certain of the cases requiring insulin The rest are given instructions about their diet and a diet sheet as a guide and some patients, such as heavy workers, take a free diet covered by an adequate dose of insulin.'

I allow a free diet with the exception of actual sugar

'I find that the majority of young diabetics require a fairly strict prescribed diet. Over 35 provided the diabetes is not very severe I allow a modified free diet—i.e. no sugar jam sweets, chocolate or potatoes, and limited bread and cake. I find with a simple diet on these lines one gets more coöperation and I am satisfied the patients take it much better than if they are on a very strict diet, to which I feel they seldom adhere.

We teach a strict carbohydrate control. The protein can look after itself and in fact, few patients can be encouraged to take enough fat Many patients adopt a completely free diet in spite of our advice and where this is regulated by insulin there is a considerable weight increase amounting to sometimes a stone a year I think a completely free diet is wrong, even in children.'

Yes: a strict dietetic régime with a fixed daily amount of carbohydrate Laxity certainly not, but freedom yes. Freedom from too small a diet. Many of our diets for a working man will contain between 200 and 300 g of carbohydrate so approaching the figure described as a free diet. As so many patients will take a liberty if given the slightest encouragement, even on generous diets the attitude of laxity is never encouraged

I advise a strict dietetic régime for all the younger and more severe diabetics, although I use a list of food exchanges to get a considerable variety in the diet. I do not think it matters much with old and mild diabetics, as long as one keeps them slim. I cannot get adequate control with a completely free diet and insulin without hypoglycæmic accidents.'

Testing of Urine

Question (*h*)—Do you encourage your patients to test their own urine at home?

The answers were almost equally divided between 'Yes' and No.'

Typical answers were:

I only encourage those people to test their urine at home who are insulin-sensitive and in whom I want information about the causes for any instability Most hospital patients do more harm than good by testing urine! In any case they do not realise that the renal threshold varies very much and they worry unnecessarily if they have a low threshold."

'I insist that all patients test their own urine at home, not only for sugar but in many cases for ketones as well.

If the patients do not test their own urine we arrange for the District Nurse to do so Otherwise how can there be any day to-day control of a diabetic?'

"On the whole we do not encourage patients to test their urine unless we are rather apprehensive about hypoglycæmic attacks, when, after a succession of [illegible] tests of the urine we get them to attend again [illegible] blood sugar, and lower the dose I have found it of value in people who are not sticking to their diet when a [illegible] of red tests will alarm them and make them [illegible] better"

Driving of Vehicles

Question (*i*).—Do [illegible] patients taking insulin drive public service [illegible] vans, [illegible] engines, tractors, [illegible]

Comprehensive yes
Comprehensive no
Qualified [illegible]
Not a [illegible]
No [illegible]
Di[illegible]

[illegible] Lawrence [illegible]

[illegible]

In London I believe it is a principle that no public-service vehicles may be driven by a diabetic receiving insulin, however well controlled, and the same applies to passenger railway engines However, I have a few engine-drivers engaged on shunting, &c , and many patients drive private cars "

"Among our patients are considerable numbers who drive ublic service vehicles, &c It has always been a matter of anxiety to us, but if they have already been in such employment we take no steps to get them out of it, and curiously enough among all these patients for many years I cannot recall a single fatality as the result. We certainly allow our ordinary diabetic patients to drive private motor-cars."

"There is no question of *allowing* diabetic patients to do these things One is not able to stop them. I have managed to persuade one unstable diabetic to give up driving a charabanc from Oxford to London. My own view is that in an ideal world diabetics on insulin would not be allowed to drive any vehicles "

A Personal Opinion

By good control of diabetes I mean the preservation of wiry and spare physique with an alert and virile emperament as the first consideration Moreover, the patient's fellow workers should be unaware that he or she is a diabetic There should be no diminution of activity in work or play and the metabolic regulation should ensure that there is complete freedom from ketosis and not more than a trace of sugar in the early morning urine The blood-sugar fluctuations throughout the day should correspond to the normal fluctuations, meaning that the blood-sugar at 11 30 A.M. should be between 100 and 150 mg per 100 ml There must be complete freedom from hypoglycæmic symptoms and physical examination must be regular and thorough.

The diet must be well within the patient's capacity nd appetite, and it must be palatable, readily obtainble, and consistent with the patient's mode of life oreover, it must be thoroughly understood and the amount of latitude in the diet must be appreciated by every patient The patient must maintain skill and care with diet but he must avoid an obsessional preoccupation with grammes and calories

The optimum weight having been obtained, usually by some reduction in the early days of training, there must not be more than two or three pounds variation through the year

I do not attain this ideal state in all my patients but this is my aim and my plan and my policy

I wage war on loose and inaccurate syringes and I believe the future will bring forth some sort of locking device for a syringe whereby a patient need not peer at markings Alternatively, it may be possible in the future to give insulin by cartridges of different strengths by a 'Mitrex' syringe

With regard to diabetics driving trains, cars, and ublic service vehicles, I believe that a heavy responbility lies upon the employers, who are entitled to full disclosure Very little can be added to Lawrence's rules (Lawrence 1952)

I do not on the whole encourage patients to test their own urine at home, save in very special circumstances I am convinced that the majority of diabetics confuse and harass themselves by home tests I prefer my patients to have thoroughgoing tests fairly frequently by attendance at my clinic, bringing two specimens at each attendance and having blood-sugar tests during the morning

I do not give out any form of standardised instruction card or sheet, but I have devised two sheets which form the basis of my individual teaching One is comparatively umple and shows the patient how to take accurate ortions of bread, sugar, and potatoes per day, together ith simple guidance as to special foodstuffs and a number elementary warnings. My other card is much more borato and enables a severe diabetic, or the parents a , a diet according to my prescription

with considerable nicety and variety. With my second card a most accurate and carefully planned diet given and I believe this is the backbone of the of diabetes mellitus

One last word. When glycosuria is found the should be sent to a clinic at once, before any diet prescribed, so that the diagnosis can be beyond all doubt.

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INTRAVENOUS PROCAINE IN THE TREATMENT OF CHEST-WALL IN

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PROCAINE has been used intravenously for the of many types of pain, and for various other conditions (Mushin and Rendell-Baker 1949) Nearly always, however, it has been given, by intravenous infusion of a dilute solution, to inpatients. I report here a trial procaine for the relief of pain associated with chest-wall injuries treated in a casualty department The procaine was given by "straight-in" intravenous injection.

First Series

Selection of Cases

Patients were chosen who were having severe pain after injury to the chest wall. The injury was often relatively minor, though some cases of major trauma were also included The pain was of three types—localised to the site of injury, diffusely spread over a wide area of the chest, or referred forwards along the intercostal nerves. In all the cases the pain was dominant and persistent, coughing, inspiration, and movement of the trunk or upper limb were often much restricted.

Technique

The procaine was injected into a vein of the forearm from a 20-ml. syringe. After various modifications, the standard dose adopted for a normal adult was 20 ml. of 1% procaine, with adjustment for age and physique. At first the injections were given slowly over fifteen minutes, but, as speed increased with confidence, the time was reduced to five minutes With stronger solutions or more rapid injection, patients became uncomfortable.

These amounts accord with the optimal dose calculated by Graubard et al. (1948) and named by him 1 procaine unit—4 mg per kg body-weight in twenty min (e g , 250 mg or 25 ml. of 1% procaine in a man weigh 10 st (140 lb)

Safeguards

Procaine has two main toxic effects—namely, co vulsions (which may lead on to respiratory paral and peripheral vascular failure resulting from medullary depression Martin (1928) attributed both these manifestations to idiosyncrasy Measures were taken to counteract these effects if they appeared A special tray was at hand containing thiopentone to antagonise the convulsant action of procaine (Clark 1942) and ephedrine to combat the medullary depression (Isenberger 1949) But in giving 82 injections there was no need to use these drugs.

Each injection was given with the patient recumbent, to counteract the vasodilator effect of procaine He then rested half an hour was reviewed, and was sent home by ambulance He was seen again next day and again a few days later

The procaine was specially prepared in separate sealed 20-ml ampoules with five-day tests of sterility and contained no adrenaline or bacteriostatic

Therapeutic Effects

The injections gave considerable relief to the great majority of patients. The pain was reduced and the general condition improved.

The degree of local relief was estimated by watching the patient, by asking him to describe any change in his symptoms, and by measuring the maximum respiratory excursion before and after injection

The pain seemed to be relieved in stages. Many cases enjoyed *immediate* relief during or immediately after injection. Others experienced *delayed* relief hours later A third group found *continued* relief during and for many hours after injection

The duration of relief varied from two- to forty-eight hours or even longer in some cases the pain never returned. On the average the pain was relieved for twenty hours, and then returned in a much milder form In some cases a second injection was given a few days later but it always seemed less effective

The main relief was usually in the diffuse severe pain occurring over a wide area. After injection the patient could breathe deeply move freely and cough Many were helped to a full night's sleep and could resume work The pain that remained or returned later was always milder localised to the site of injury and susceptible to local methods of relief

The general condition improved beyond what might be expected purely from the alleviation of pain Patients lost their depression and became cheerful or even frankly euphoric This effect was often associated with immediate relief of pain

Thus procaine may act both centrally on the cerebral centres—an immediate effect—and peripherally by direct action at the site of trauma giving delayed relief

Toxic Effects

About half the patients experienced mild discomfort —e.g dizziness, a feeling of warmth or burning all over a feeling of numbness or deadness, twitchings in the muscles, or temporary loss of the power of speech. These symptoms seemed to be related to the speed of the injection and never lasted more than a few minutes. One patient lost consciousness, at the end of the injection for about two minutes but was none the worse after consciousness returned

No evidence of a delayed toxic action was found in the sample of patients followed up for a year

Physiological Effects

The pulse-rate was found to slow by an average of 8–10 beats per minute during the injection, but there was no change in volume. The blood pressure fell by an average of 10 mm Hg systolic and 5 mm. diastolic the fall being proportionally the same in 2 established hypertensives. Vasodilatation of the cutaneous vessels commonly showed as generalised flushing towards the end of the injection, associated with a feeling of warmth, and in these cases there was a rise of 1–2°F in other cases the temperature remained unaltered

Results

In this first series, 50 injections were given to 43 patients, with the results shown in table I It appeared (1) that intravenous procaine injections, given as described, are effective in relieving the acute pain of chest-wall injuries and (2) that the pain of fractured ribs is relieved more fully than that of soft-tissue injuries This agrees with the findings of Batcher (1948)

TABLE I—FIRST SERIES 50 PROCAINE INJECTIONS IN 43 PATIENTS

—	Fractures (36 injections in 29 patients)	Soft-tissue injuries (14 injections in 14 patients)
No relief	8 %	44 %
Moderate relief	62 %	36 %
Great relief	30 %	20 %

TOXIC EFFECTS

None 44% Mild 54% Severe 2%

Second Series

It could be objected however that though the injections seemed to relieve most patients procaine was not necessarily responsible for the relief The patient, lying on a couch and receiving a protracted injection was under a strong hypnotic influence to which the benefit might be partly or entirely attributed A control series was therefore treated to ascertain how far the procaine was responsible

Two sets of 20 ml ampoules were prepared, identical and unmarked, one containing 1% procaine and the other containing physiological saline and these were placed in separate labelled boxes All injections were given by me but the ampoule I used was selected for me by a person with no knowledge of the case I recorded the effects of the injection without knowing the nature of the fluid injected, nor did I look at the key list (showing which ampoules had been used) until I had completed and analysed my observations.

In this series 53 injections were given to 40 patients, 32 receiving procaine and 21 physiological saline Results were again graded according to the measure of relief (table II) and adverse effects were noted. It is evident *that procaine injections gave far greater relief* Of the saline group 4 (19%) noted great relief—presumably being susceptible to the suggestive effect of the injection—and 11 (53%) were unaffected Of the procaine group 12 (36%) noted great relief, and only 5 (16%) were unaffected

TABLE II—SECOND SERIES: 53 PROCAINE OR SALINE INJECTIONS IN 40 PATIENTS

—	Saline (21 injections)	Procaine (32 injections)
No relief	53 %	16 %
Moderate relief	28 %	48 %
Great relief	19 %	36 %
TOXIC EFFECTS		
None	68 %	57 %
Mild	32 %	43 %
Severe	0 %	0 %

Of the 32 patients treated with procaine 2 lost consciousness for a few minutes, and 1 lost the power of speech and showed mental disorientation for ten minutes.

All 3 quickly returned to normal, and experienced continued relief of pain. In 2 of the procaine patients, both elderly men, the pulse became markedly irregular for about an hour, returning to normal without further cardiovascular disturbance neither had any obvious heart lesion

The patients treated with saline solution showed a lowing of the pulse similar to that seen with procaine, ut they did not show lowering of blood-pressure or ising of temperature.

The beneficial effect of the procaine was found to be greater in the second than in the first series The reason may be that the selection of cases with acute pain was stricter in the second series—i e, there was a higher proportion of the type of case most relieved by procaine Of the 32 procaine injections in the second series, 6 were second injections, now recognised as having less effect than the initial injections Procaine was again more effective in fractures than in soft-tissue injuries, whereas the relief given by saline solution was equally divided between the two

The second series establishes that procaine is the effective agent in the relief of pain Thus relief varies with

1 *Type of injury*—Fractures benefit more than soft-tissue injuries.

2 *Temperament*—The phlegmatic patient gains greater nd more prolonged relief than the sensitive

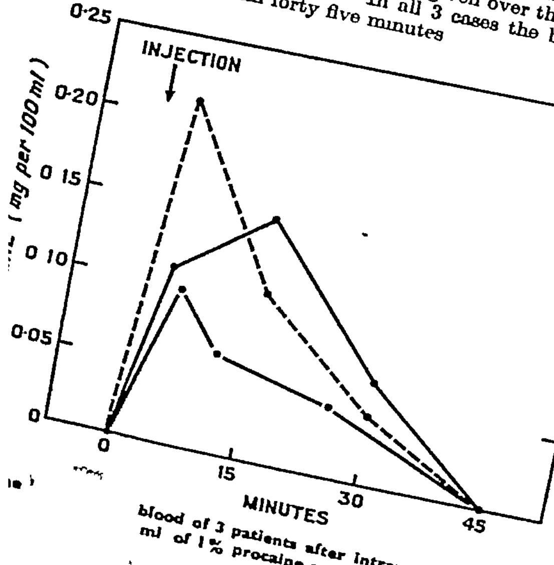
3 *Nature and degree of pain*—The more acute and generalised the pain, the greater the response

4 *Time-interval following injury*—The relief is greatest when injections are given within a few hours of injury With delay the pain seems to become "established" and the effect of procaine progressively less.

Suggested Mechanism of Pain Relief

The duration of relief afforded by intravenous procaine appeared surprisingly long Accordingly, procaine metabolism in the body was studied by estimating rocaine levels in blood and urine after injection The ollowing biochemical estimations were carried out by r R Gaddie, whose helpful advice was much appreated.

Blood procaine levels were measured in 3 patients, using a odification of Bratton and Marshall's method (Graubard et al 1947) Procaine in the serum rises to its peak within minutes of injecting (see figure), the injection given over the shortest time attains the highest level In all 3 cases the blood was free of procaine within forty five minutes



blood of 3 patients after intravenous injection ml of 1% procaine solution.

Urinary estimations were carried out in 3 cases amount of procaine excreted during the first hour was tively 7·7 mg, 1 1 mg, and 2·1 mg Excretion of after the first hour was negligible This confirms the of animal experiments showing that procaine is broken rapidly in the blood by procaine esterase, and by the liver the tissues (Lee 1947)

Thus procaine remains in the blood-stream than one hour, yet its effect may endure for days suggests that the relief of pain is due to abolition of vicious circle of pain→muscle spasm→pain, rather than to the purely local anæsthetic action.

Pulmonary complications such as collapse and monia are common following chest-wall injuries, larly in the elderly. As procaine given in the acute stage increases freedom of respiratory movement, its use should help to prevent these It should not, however, be given to elderly patients myocardial weakness, cardiac arrhythmia, or heart (Miller et al. 1952), or, of course, to patients known to sensitive to procaine

Summary

In a casualty department patients with chest injuries have been given intravenous injections of 1 procaine solution in the hope of reducing pain muscular spasm and thus improving respiration standard dose for a normal adult was 20 ml, in during not less than five minutes

Precautions are required against convulsions peripheral vascular failure, but these were not seen after any of the 82 procaine injections given. In 3 cases patient lost consciousness, and in 2 the power of was lost, but these effects were transient. In 2 men the pulse was irregular for an hour

Pain was greatly or moderately relieved in the large majority of the patients, and their respiratory and general condition improved The relief was greater in cases with fractures than in cases with only soft injury, and the benefit was greatest when the in was given soon after the injury In some cases the was immediate, in others it was delayed for a hours It lasted on the average for some twenty hours A second injection was never as effective the first.

Estimation of procaine levels in blood and urine an injection confirmed previous observations that procaine is excreted from the blood within an hour. Its effect over a period of hours or days is probably not due to any continuing anæsthetic action but to a breaking of the vicious circle pain→muscle spasm→pain.

In a small series of control cases, intravenous injections of physiological saline were given under exactly similar conditions Some benefit was evident, but it was much less than with procaine, and it was not greater with fractures than with soft-tissue injuries

I should like to thank Mr A. B Watson, director of the casualty department of the General Hospital, Birmingham, for suggesting that I should try intravenous procaine in these cases and for his great help and encouragement I am indebted to Mr R Gaddie, PH D, for the procaine estimations, and to Mr C McArdle and his staff for preparing the ampoules. The work could not have been completed without the help of my medical colleagues and the nursing staff in the casualty department

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TWO CASES OF MYXŒDEMA ATTRIBUTED TO IODIDE ADMINISTRATION

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The effect of iodide on the mammalian thyroid gland is curious and even paradoxical. When the quantity ingested is below a certain level (about 0·1 mg. daily in man) the gland cannot make adequate quantities of its hormone, and clinical hypothyroidism may develop. It has also been shown, both in the rat (Wolff and Chaikoff 1948) and in man (Stanley 1949, Childs et al. 1950) that single doses of iodide above a certain level (probably about 5 mg. in man) also prevent formation of the hormone, at least temporarily. This experimental observation may explain at least in part, the well known clinical fact that patients with thyrotoxicosis improve when given iodides. However, in such cases inhibition of the production of thyroid hormone is insufficiently complete or long lasting to produce clinical myxœdema (as it can be when drugs of the thiouracil series are administered), and in non-thyrotoxic subjects there is no recorded instance known to us of clinical hypothyroidism resulting from the administration of iodides.[1] We describe here two cases in which we believe that this happened.

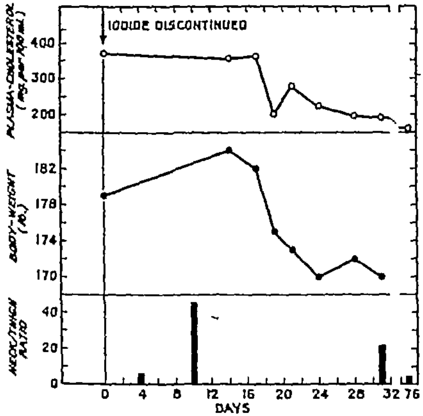

Fig. 1—Plasma-cholesterol, body-weight, and radio-iodine uptake in case 1 after iodide-containing cachets had been discontinued. Radio-iodine uptake was measured as the ratio of neck count to thigh count at two hours after administration of a tracer dose (normal range 1 to 10).

Case records

Case 1.—A man aged 66 underwent in 1945 resection of the colon for carcinoma. In 1950 he had been referred to the radiotherapy department of University College Hospital for treatment of a possible metastasis in the spine. During this treatment it was noticed that he was becoming slower, his face was becoming puffy, and his speech was indistinct. These changes were first noticed in January 1951. He was referred to Prof. M. L. Rosenheim, who diagnosed myxœdema and arranged for his admission to hospital.

On admission on June 29, 1951, the diagnosis of myxœdema was quite obvious. His face was pale and puffy, his skin dry, harsh, and cold, and his speech slurred. The thyroid was not palpable. The basal metabolic rate (B.M.R.) five days after admission was −15% and the plasma-cholesterol level 370 mg. per 100 ml.

Progress.—About a week after admission (no treatment having been given) it was noticed that he was becoming more alert and his face less puffy. Accordingly all treatment was withheld, and the signs of myxœdema gradually disappeared. Twenty-one days after admission the B.M.R. was −2% and the plasma-cholesterol level 200 mg. per 100 ml. (fig. 1).

Investigation.—The first radio-iodine study was done four days after admission. This was only a brief routine test and showed a neck/thigh ratio[2] of 6·5 at two hours after administration of a tracer dose of radio-iodine. This was well within the normal range of 1 to 10. More remarkable was the fact that the neck/thigh ratio at twenty-four hours after the administration of the radio-iodine was still 6·0. The significance of this observation was not appreciated at the time, but can only mean that all the radio-iodine in the thyroid must have been in the form of iodide. In other words, hormone formation must have been completely blocked at this time, as it would have been had the patient been taking large doses of thiouracil. Under these conditions a figure of 6·3 for the neck/thigh ratio indicates a fairly large thyroid iodide space such as is found in hyperplastic glands.

A second radio-iodine test was made six days later (ten days after admission). This gave a result totally different from that of the previous test. The neck count rose steeply, and two hours after the radio-iodine was given the neck/thigh ratio was 46·3. The peak uptake was at twenty-two hours and amounted to about 87% of the administered dose. The urine passed during the twenty-four hours contained only 5% of the dose. The neck counts were observed during the succeeding days. During the first four days they fell rapidly at a rate of 11% per day (euthyroid subjects usually have a rate of fall of 0–2% per day); then the rate diminished and ceased to be exponential. A sample of serum taken twenty-four hours after the radio-iodine was given contained 0·7% of the dose per litre, of which 90% was protein-bound. Thereafter the serum radioactivity increased rapidly, reaching a peak value of 2·9% per litre. Thigh counts, after an initial fall, rose in parallel (fig. 2). All these findings are what one would expect to find in well-marked thyrotoxicosis. The rise in serum and thigh counts in the days following the tracer

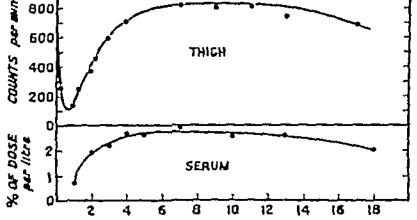

Fig. 2—Changes in counting-rate of neck and thigh regions, and of plasma aliquots, after a tracer dose of I¹³¹ administered ten days after discontinuation of iodide-containing cachets (case 1).

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[1] Bell, cited by Werner (1953), appears to have encountered similar cases, but the text of his report to the American Goitre Association is not yet available in this country. Haben (1953) has recorded the development of myxœdema and goitre in a patient who had had a bronchogram. The inhibition of the thyroid was attributed to the absorption of iodide from the radio-opaque oil.

[2] Counting rates were measured with a Geiger counter 16·5 cm. from the neck, and another similar counter between the thighs.

dose [illegible] represents an outpouring of radioactive thyroid hormone into the blood

A third radio iodine test, done thirty one days after admission, gave a two hour neck/thigh ratio of 21 7 (still above normal limits) After this dose the neck counts fell at a normal rate (0 2% per day), and there was no secondary rise in thigh count

A fourth test done seventy-six days after admission gave a normal two hour neck/thigh ratio of 4 4.

It was apparent that at the time of admission the thyroid was being prevented from making its hormone by some unidentified agent This agent ceased to act soon after admission and the thyroid was then released and showed a very high turnover-rate Subsequently thyroid function gradually returned to normal This sequence of events would have been exactly reproduced if the patient had taken large doses of thiouracil continuously for many months up to the time of admission This would have caused hypersecretion of thyroid-stimulating hormone, with consequent hyperplasia of the thyroid If the thiouracil had been stopped at the time of admission, the thyroid would have been once more able to make hormone and, being hyperplastic, would have done so at an abnormally high rate As the level of circulating hormone rose, less and less thyroid-stimulating hormone would have been formed, and thyroid function would gradually have reverted to normal The patient was therefore closely questioned about any medicaments he had been taking The only one he had been taking constantly for long periods consisted of cachets for rheumatism, made up according to a formula given him by a previous private doctor

Powdered cinchona gr 3
Powdered guaiacum resin gr 6
Powdered ammonium carbonate gr 2
Powdered lithium carbonate gr 2
Potassium iodide gr 1
Powdered colchicum gr ¹/₈

The dose was one cachet t d s He had started taking this before the war and, apart from two years during the war (when he was unable to obtain it), had continued to do so regularly and continuously up to the time of admission. He took none while in hospital

A review of the constituents showed that none (apart from the potassium iodide) were known to have any anti thyroid action This was confirmed as follows

Experiment—100 mg of the mixed powder (but excluding the potassium iodide) was suspended in water and given to each of five rats (each weighing about 100 g) by stomach tube This dose amounted to slightly less than the patient's usual daily dose, or about 700 times his daily dose on a body weight basis An hour later these five rats, and five control rats, were each given 5 μC of I^{131} intraperitoneally They were killed three hours later, and their thyroids were digested in 10% sodium hydroxide and counted in a liquid counter In both treated and control rats the mean thyroid content of radioactivity amounted to 34% of the administered radio iodine The patient's daily dose of potassium iodide was 180 mg (136 mg of iodide)

Follow up—After the patient left hospital he started taking the cachets once more in the same dose After nine months his weight increased by 13 lb and his plasma cholesterol level rose from 160 to 240 mg per 100 ml There were no obvious signs of myxœdema He then discontinued the cachets, and a week later a radio iodine test gave a two hour neck/thigh ratio of 27 0 Thirty three days after the cachets had been discontinued this had reverted to a normal level of 7 8 These observations suggested that his thyroid had once more become hyperplastic while he was aking the cachets and that this had enabled it to produce nough hormone to prevent gross myxœdema

At about this time the patient developed progressive undice which ended in his death a year later

Necropsy Findings—Deposits of secondary carcinoma were und in the abdominal lymph glands and the liver was ssly cirrhotic The thyroid was diffusely enlarged, weighing g examination showed a very uniform large acini distended with colloid and lined There was no lymphocytic infiltration.

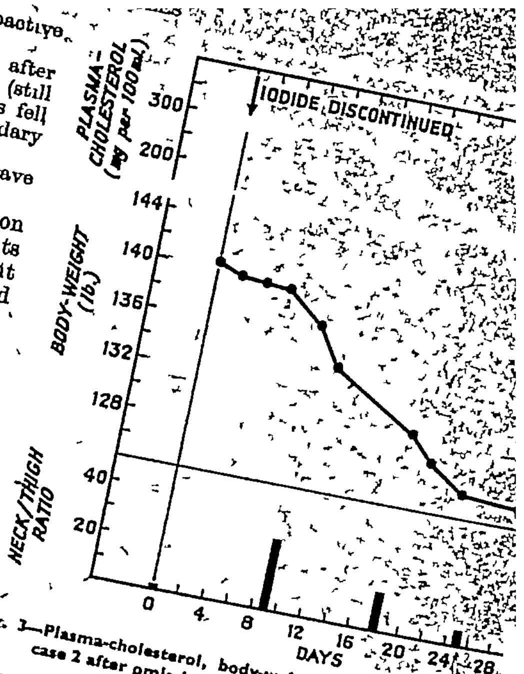

Fig. 3—Plasma-cholesterol, body-weight and radio-iodine up
case 2 after omission of iodides from an asthma mixture

Case 2.—A housewife, aged 45, was admitted t Elizabeth Garrett Anderson Hospital, complaining backache and a gain of one stone in weight in three four months She had noticed swelling of her abdom face, and hands for six weeks, and that she tired a felt the cold more easily than before Her voice become husky over the last few weeks She known asthmatic, and it later transpired that she been in the habit of taking a mixture containing gr of sodium iodide[3] (423 mg of iodide) at least four h and sometimes more often over the last four years

On examination she was pale and lethargic, with much puffiness round the eyes and œdema of both legs, reaching the knees and pitting with difficulty The skin was and cold. There were occasional rhonchi in the lungs The thyroid gland was easily seen and felt, it was enlarged and extremely firm on palpation, it was abnormally vascular and moved easily on swallowing

A clinical diagnosis of myxœdema was made, associated with a Hashimoto thyroiditis, because of the firm enlargement of the gland

Investigations on admission supported the diagnosis, the B M.R being −21% and the plasma-cholesterol level 300 mg per 100 ml Radiography of the chest showed a heart shape compatible with myxœdema.

Treatment and Progress—As the ingestion of large dos of iodide was a common factor in both cases 1 and 2, it w decided to omit the iodide from this patient's medicines, a other constituents remaining the same This was followed by a dramatic change in the clinical state over the ensuing three or four weeks The œdema and puffiness disappeared the body weight falling from 140 to 126 lb, with a diuresis maximal on the sixth day after withdrawal of the iodide The patient became more alert, her skin finer and warmer and her thyroid gland very much smaller and softer, with the result that at the end of this time it was difficult to feel The plasma-cholesterol level fell from 300 mg per 100 ml to 150 mg per 100 ml (fig 3) Unfortunately a final B.M. reading was unobtainable because the patient went into status asthmaticus on withdrawal of the iodide Radiography of the chest showed considerable reduction in the heart at the end of the period (fig 4)

Radio iodine measurements made before withdrawal of the iodide and at intervals afterwards as in case 1, were follows

	Neck/thigh ratio	*Dose of radio-iodine in thyroid at 24 h*
Before withdrawal	0 75	1 7
9 days after withdrawal	27-30	79
18	15 95	63
25	7 50	[illegible]

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[3] Potassium bromide gr 5 Liquid extract of liquorice minims 1 Chloroform emulsion minims 7 Caffeine iodid

These results showed a similar trend to case 1. There was a practically zero uptake at two and twenty-four hours on the day following withdrawal of the iodide. Nine days later these measurements were in the thyrotoxic range, suggesting a hyperplastic thyroid gland. Eighteen days after withdrawal of iodide the levels had fallen, but they were not within the normal range until twenty-five days. At the end of this time the patient was in a severe status asthmaticus and for psychological reasons we were forced to administer iodide again in the exact mixture as before. Within a week the thyroid gland became easily palpable and very firm.

It therefore seemed that in this case also the iodide had an anti-thyroid action, causing blockage of formation of thyroxine and consequent hyperplasia of the gland and myxœdema.

The patient has now been discharged taking her medicine. She will be given thyroxine if evidence of myxœdema appears; for it seems unlikely that she will be willing to give up her iodide mixture.

Discussion

In case 1 the signs of myxœdema disappeared shortly after the patient was admitted to hospital although no treatment had been given. Four days after admission his thyroid gland could concentrate iodide but not make hormone. Six days later radio-iodine studies showed that iodine was passing through the thyroid and emerging in the blood in protein-bound form at an abnormally high rate—in fact at a rate commonly found in thyrotoxicosis. Some weeks later, when all signs of myxœdema had disappeared, the radio-iodine uptake gradually returned to normal. These studies strongly suggest that thyroid function had been severely depressed and then suddenly released, with a period of rebound overactivity. Thyroid function was released from four to ten days after admission to hospital. Since the patient's diet at home did not differ much from the hospital diet, the most likely reason for the release of the block to the thyroid on coming into hospital was that he had ceased to take his cachets from the time of admission. It might still have required from four to ten days to reduce his blood iodide to a level at which it would not affect thyroid function. Further evidence that the cachets were responsible was obtained from the temporary increase in radio-iodine uptake seven days after the end of a second course of cachets. The constituents of the cachets, other than potassium iodide, were shown to have no anti-thyroid action in rats. The evidence therefore pointed to iodide as the cause of his myxœdema.

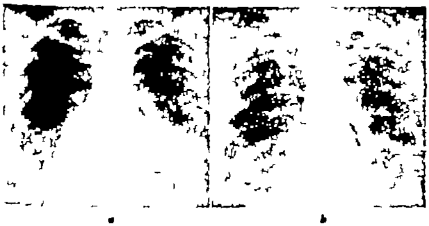

Fig. 4—Size of heart in case 2: *a*, while the patient was taking iodide-containing mixture; *b*, 14 days after omission of iodides from the mixture.

In case 2 the removal of the iodide from the asthma mixture without any other change, led to the same sequence of events. The signs of myxœdema disappeared, and the uptake of radio-iodine which had been nil became supernormal and then gradually returned to a normal value, suggesting a phase of rebound overactivity as thyroid function was released. Since the potassium iodide was only discontinued after a period of observation in hospital and was the only constituent removed from the asthma mixture it seems highly probable that it was the agent responsible for suppressing thyroid function.

In case 2 a moderate-sized firm goitre had been present when she was myxœdematous. After the iodide was discontinued, the goitre rapidly became smaller and softer. When iodide was restarted the goitre again became more obvious. The presence of the goitre is interpreted as an attempt to overcome the difficulty in making thyroid hormone.

In view of the experimental observations of Wolff and Chaikoff (1948) and Stanley (1949) it is perhaps surprising that no other instances of myxœdema attributable to iodides appear to have been recorded. One reason, no doubt, is that a diagnosis of myxœdema is usually followed automatically by the administration of thyroid extract, without a search being made for a possible causal agent. Even if an allowance is made for this, it seems certain that other cases would have been recognised if the exhibition of iodides commonly caused myxœdema. It seems much more likely that the human thyroid becomes in some way tolerant to high blood-iodide levels, as is suggested by the work of Wolff et al. (1949) in rats. They showed that when high blood-iodide levels were maintained the thyroid's capacity for binding iodine returned during the course of a few days. This experimental observation is not necessarily relevant to the state of patients who are taking iodides, since their dosage is unlikely to be as regular and as evenly spaced throughout the twenty-four hours as that of the rats. A fall of the blood-iodide level below the critical level for blocking organic binding might have effects in opposite directions according to the interval between doses. On the one hand intermittent dosage might prevent the development of tolerance to iodide. On the other hand, if the intermissions were long enough, the thyroid might be able to produce enough hormone intermittently to prevent myxœdema. The fact that both our patients had been taking iodides for several years before myxœdema appeared, and that case 1 did not develop gross myxœdema within nine months of resuming iodides, suggests that the formation of thyroid hormone was not continuously suppressed in either patient.

Keating et al. (1950) found normal values for radio-iodine uptake in 21 euthyroid persons about a week after discontinuing heavy doses of iodides. It can therefore be presumed that their thyroids had not become hyperplastic. In most instances the normal thyroid can apparently evade the blocking action of iodides. Our two patients seem to be peculiar in that their thyroids could not do so.

Summary

In two patients with myxœdema the symptoms and signs disappeared on discontinuing iodide-containing medicaments which they had been taking for many years. In one case a goitre was present, and this became much smaller.

Radio-iodine uptake, measured nine and ten days after discontinuing iodide, was in the thyrotoxic range in both cases. A few weeks later it had returned to normal in both cases.

The myxœdema is ascribed to the anti-thyroid action of iodides.

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ALOPECIA, OPTIC ATROPHY, AND PERIPHERAL NEURITIS OF PROBABLY TOXIC ORIGIN

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THE association of alopecia, optic atrophy, and peripheral neuritis in the same patient is in itself remarkable, and, in the light of recent additions to our knowledge of the ætiology of the peripheral neuropathies (Elkington 1952), suggests a selective biochemical disorder In the present case the illness began acutely with vomiting and diarrhœa, and the occurrence of these symptoms at the same time in other members of the household, followed in one case by alopecia, is evidence of a common toxic cause.

Case-record

A housewife, aged 59, was admitted to Guy's Hospital in September, 1950, with loss of vision, loss of hair, and pains in her legs She was a trained nurse and a doctor's widow She had been liable to attacks of depression since 1943, when she was living alone in the Midlands, and in October, 1948, had attempted to commit suicide by taking morphine. In June, 1949, she moved into a flat at the top of her son in law's house in Surrey

Beginning of Illness

Her illness began in July, 1949 On the 15th there was a family reunion luncheon in the patient's flat, attended by her son, her married daughter, and her son in law (who are all doctors) and their child. About twelve hours later the patient began to vomit, with some diarrhœa and abdominal colic. These symptoms continued for two days and were followed by nausea and anorexia for a week. At about this time, and during the next two weeks, the hair of her scalp and eyebrows fell out progressively until she was completely bald On July 31 she developed tingling and shooting pains in her feet, hands, and scalp, these became worse until she could neither walk nor sleep

Son's Illness

About forty eight hours after the luncheon on July 15 her son developed general lassitude and aching in his legs About a week later most of his scalp hair fell out and it took about three months to grow again. At the same time his sister, her husband, and their child had vomiting and diarrhœa for about two weeks

First Investigation and Treatment

On Sept 5, 1949, the patient was admitted to another hospital after an exacerbation of vomiting She had complete alopecia of the scalp and eyebrows and hyperæsthesia of the toes and her leg reflexes were sluggish. A blood count showed severe polymorph leucocytosis but no anæmia. The blood-urea and blood sugar levels were normal, and lumbar puncture produced normal cerebrospinal fluid under normal pressure

Thallium poisoning was diagnosed, although examination of the urine and fæces and muscle biopsy revealed no trace of this metal The patient was given a course of dimercaprol in the dosage recommended by the Medical Research Council (1947) The pains began to regress during the following few days but at the same time her vision started to deteriorate rapidly being reduced in about two weeks to 6/60 in each eye After another two weeks her visual acuity began to improve, and her hair to grow again, but unfortunately she became increasingly depressed and had to be removed to a mental hospital for a while, after which she seemed restored to a reasonably happy state of mind

Maid's Illness

She returned home in December, 1949 In January, 1950, a maid working in the patient's flat had a short attack of diarrhœa and vomiting followed by loss of hair

Patient's Relapse

The patient continued to improve, and by March, 1950, she could read large print examination of her fundi at this time showed slight optic atrophy In July, 1950, however, her vision rapidly deteriorated again, and about two weeks later her hair began to fall out and she developed severe paræsthesiæ in the lower legs, scalp, and abdomen.

Further …

On … to Guy's Hospital on Sept 12 1950, she was … bald Her eyebrows were also affected, but not her pubic or axillary hair Her vision was so poor she could not identify a hand if it was held more than … away from her eyes, and the fundi showed bilateral … atrophy There was slight hyperæsthesia of both calves … deep pressure, and possibly some reduction of vibration … in the feet. She was naturally anxious about the loss … vision but otherwise did not seem to be unduly depressed … blood-count showed slight polymorphonuclear … A test-meal showed normal gastric acidity and emptying, … blood urea and serum protein levels were normal

Further Treatment

Again, a clinical diagnosis of thallium … although no trace of this metal was found in samples of … nails, and urine However, the patient had impa… tolerance, which seemed to support a diagnosis of heavy … intoxication (Joiner et al 1950) Accordingly she … another course of dimercaprol in higher dosage than … (4 ml of a 5% solution intramuscularly q d.s. for four … then 4 ml. t d.s. for four days, and then 1 ml daily for … days) After five days' treatment pyruvate tolerance … normal, but no heavy metal was detected in the urine … this period, in spite of repeated attempts The … paræsthesiæ gradually disappeared during the treatment … her hair started to grow again. Her vision improved slight… and when she was discharged on Nov 20, 1950, her … acuity was 1/60 Since then, however, there has been … progress.

Search for a Poison

Careful search was made at the patient's home, b… the incident in July, 1949, and again in 1950, but … known to contain thallium (or other heavy metal) wa… After the first incident all the patient's culinary … utensils were changed, and the water in the house's … tanks was analysed with a negative result.

Discussion

From this lady's story, and the fact that other … of the household were affected, it seems reasonab… assume that this was a case of recurrent poisoning … are very few substances which will cause alopecia, … alone one as complete as this. Alopecia areata … may occur in members of the same family, and … quite rapid in its onset, but it would be a … coincidence for it to happen in two members at the … time When optic atrophy, peripheral neuritis, and … of diarrhœa and vomiting are added to the syndrome, … seems difficult to imagine as the cause any substance … than thallium salts. It is true that arsenic will … of hair as well as paræsthesiæ, blindness, and … intestinal disturbance, but it does so more gradually … effects being patchy and not so dramatic as in the … case

USES AND EFFECTS OF THALLIUM

Thallium is not in common use Commercially it … employed in a rat poison and an insecticide, and … year 1930 a depilatory cream was marketed in the U.S.A. … which caused numerous cases of poisoning (American … Medical Association 1931) and manufacture of which was … abandoned in 1932 Industrially, the liberation of … thallium in the manufacture of sulphuric acid from iron … pyrites has been reported as causing toxic effects (Buschke … and Langer 1927) It is used also in making filaments in … tungsten lamps, in some imitation gems, and in low … temperature thermometers Its therapeutic use has been … abandoned almost completely.

Thallium's toxic effects were noted very soon after its … discovery Lamy in 1862 developed peripheral neuritis … while working with the metal, which he had identified … independently of Crookes, who made his discovery the … year before (Lamy 1863a, Crookes 1861), and found that … it was lethal to animals (Lamy 1863b)

Alopecia

Combemale (1898) found that thallium caused alopecia in … patients to whom he administered it to alleviate night sweats … and at about the same time Sabouraud noted the same effect … in a person who had been given thallium to control diarrhœa … This led him to use the acetate salt locally and orally for the … treatment of ringworm of the scalp, but because of its toxicity … he soon abandoned its use in favour of X irradiation, and … advised that thallium acetate should only be …

peutically in strengths of less than 1%, and then in only small doses and at long intervals (Sabouraud 1912)

Ocular Symptoms

Kaps (1927) first noted optic atrophy in a human case of acute thallium poisoning (which in his case was preceded by retrobulbar neuritis) and since then further cases have been reported (Girot and Braun 1929 Lillie and Parker 1932) Non inflammatory keratitis (Richet 1899) and cataract (Duke Elder 1947 Castelao 1941) have also been reported.

Mental Disturbances

Mental symptoms during the acute phase have been described varying from delusions of persecution (Bachkevitch and Prokoptchouk 1929) to depression and suicidal tendencies (Greving and Gagel 1928) or even complete dementia (Kaps 1927). This might explain our patient's depression during the first episode in 1940 but she seems to have had such a tendency for long before then

Alimentary Tract

Ulcerative stomatitis with blue line albuminuria and tachycardia have also been reported (Ginsberg and Nixon 1932) and experimentally thallium seems to promote the flow of impulses in the autonomic nervous system (Dixon 1927) Diarrhœa and vomiting with abdominal colic, are typical of the acute poisoning and the fact that there was some delay between the appearance of these symptoms and the probable ingestion in the present case supports the diagnosis. Indeed it seems probable that these effects develop only after the thallium has been absorbed (Dixon 1927) because similar symptoms appear after local applications.

Blood Picture

The leucocytosis which was present during both of our patient's attacks are also consistent with thallium poisoning and on occasion thallium seems to cause anæmia also (Mamoli 1936, as a result of experiments on albino rats)

Endocrine Glands

There has been much discussion as to whether thallium has specific toxic effects on the endocrine glands, but Cox and Hodgerson (1936) have made investigations which tend to disprove this

Unfortunately we could not detect thallium in abnormal quantity in the present case but this fact certainly does not exclude the diagnosis of thallium poisoning because we could not investigate the patient at the immediate onset of the symptoms of her episodes. (The methods used for examination of specimens were spark spectroscopy and a polarographic method devised by Mr R. W R Baker) The impaired pyruvate tolerance test during the second episode in 1950 was suggestive of poisoning by a heavy metal especially as it returned to normal after treatment with *dimercaprol* (*Joiner et al.* 1950) It is difficult however to ignore the facts (1) that we could find no history of contact with thallium or any heavy metal and (2) that thallium is not in common use.

SIMILAR CASES

Euzière et al (1951) have reported three cases of recurrent polyneuritis with alopecia closely resembling that described here. These three patients were men separately observed, and without any association with one another who developed recurrent bouts of alopecia together with symptoms and signs of polyneuritis Two of them also had optic atrophy with almost complete loss of vision, and one had irritability and depression with suicidal tendencies Euzière et al considered the possibility of thallium poisoning but there was no evidence of contact with thallium, and they do not appear to have searched for it in the patients excreta.

Stiefler (1929) reported two cases of unknown ætiology with paræsthesiæ and alopecia of acute onset, associated also with painful and swollen joints. Radermeker (1944) describes two patients who suddenly developed paræsthesiæ and alopecia, one also showing optic atrophy Both patients had paralysis of the lower limbs and sphincters, isolated cranial nerve palsies, and an increased amount of albumin in the cerebrospinal fluid In none of these four cases were the attacks recurrent.

Bingel (1931) described the case of a married woman who had recurrent attacks of alopecia and of paræsthesiæ in her legs and died in the third bout Each recurrence took place when the patient returned home from hospital and owing to this and her husband's rapid remarriage after her death a necropsy was performed in which a careful search was made for thallium and arsenic, but without success. Bingel considered his case to belong to the same group as those described by Stiefler (1929) but the published case reports do not support this conclusion

In the present case the circumstantial evidence of poisoning seems reasonably strong, but the only reason why thallium has been advanced as a possible cause is that it seems to be the only substance which could give rise to this syndrome The strongest argument against this diagnosis is the failure to find any history of contact It may well be that this case (and possibly those of Euzière et al and that of Bingel) were due to some hitherto unsuspected toxic cause

Summary

The case is reported of a patient with recurrent bouts of alopecia, optic atrophy and peripheral neuritis

A comparable illness affecting at the same time other members of the household suggests a toxic cause.

The evidence for and against the diagnosis of thallium poisoning is discussed

The conclusion is reached that the syndrome may result either from thallium poisoning or from some other toxic cause at present unidentified

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INFANTS' LEGS AND THE SLEEPING POSITION

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During the latter part of pregnancy the fœtus occupies very cramped quarters in the uterus and therefore adopts a position in which it occupies the least possible volume As part of this attitude the legs are folded one upon the other the hips are fully flexed and externally rotated the knees are flexed the tibiæ are crossed one over the other and each foot is pressed on to the opposite buttock (fig 1) To maintain this position certain adaptive changes are made, and can be observed if the legs of a newborn child are examined

The *feet* lie on the buttocks, and are moulded to their surface The heels are in slight varus and the fore feet are inverted and adducted

The *tibiæ* lie crossed one over the other with the result that they are bowed laterally The bow is most marked in the

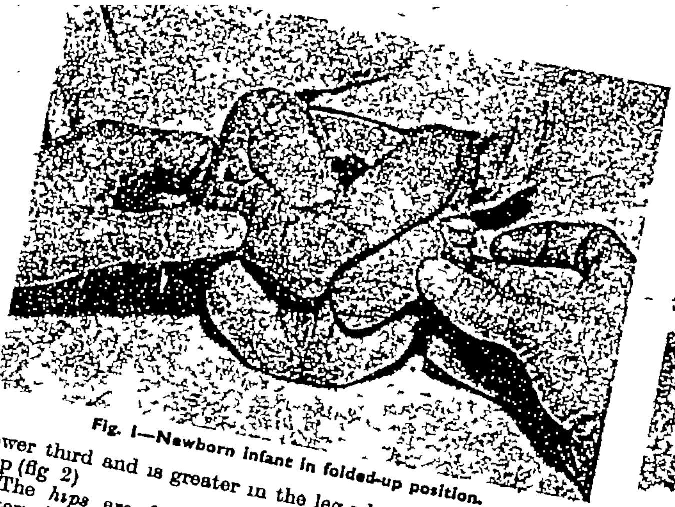


Fig. 1—Newborn infant in folded-up position.

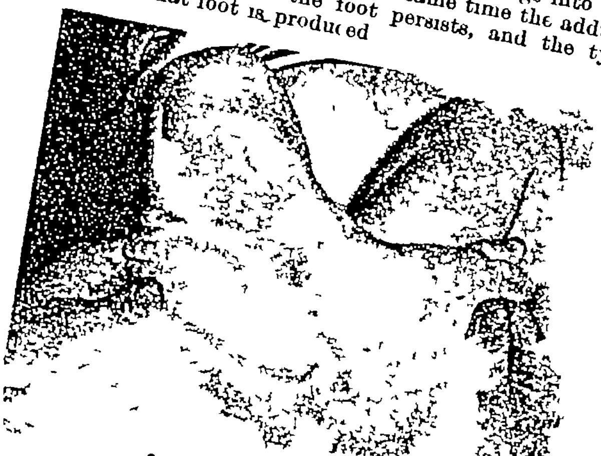
lower third and is greater in the leg which habitually lies on top (fig 2)

The *hips* are fully flexed and externally rotated Full external rotation of the hip in the young infant is, however, diminished and internal rotation is correspondingly greater than normal This altered arc of rotation is caused by an increase in the angle of anteversion of the neck of the femur on the shaft, which is present in the newborn and decreases with age (Dunlap et al. 1953) The effect is that, in full lexion and external rotation, the knees cannot fall sideways outside the line of the trunk as they would in an older child, and thus the child's volume is not increased

Many small children habitually adopt the "folded up" position during sleep, at the same time lying prone with the buttocks raised (fig 3) If this habit persists, the adaptive attitude of the legs remains, and, if the child is still sleeping in this position when it starts to walk, certain errors of stance and gait are noticeable Such a child walks with flat feet, bowed tibiæ, and an intoe gait

Infantile Flat foot

This is almost universal in the toddler Two factors are responsible The first is general, and consists of an inability to balance on the subtaloid joint, with the result that the foot collapses into valgus in exactly the ame position that a person adopts when learning to kate on ice The second is due to the fact that in the folded up position the fore part of each foot is inverted and adducted When the child places the fore part of the foot flat on the floor, the heel swings into valgus and the arch collapses At the same time the adduction of the fore part of the foot persists, and the typical infantile flat foot is produced



2 years, showing the ease with which the legs can be folded up.

Fig 2—Same infant as in fig 1, showing bowed tibiæ

Infantile Bowed Tibiæ

As has been pointed out, this is a lateral bow marked in the lower third These children are healthy and often overweight They bear none stigmata of rickets; so the common suggestion is a rickety deformity is obviously untenable

Infantile Pigeon Toes

The intoe gait of young infants has been an internal rotation deformity in the tibiæ adduction of the fore parts of the feet Th these factors may contribute, examination of of such a child will show that most of the arises at these joints

Fig 4 shows that there are increased internal and decreased external rotation at the hip This arc of rotation is due to an increase in anteversion neck of the femur, which may be as much as 80° newborn and diminishes with age The mid of rotation is on the internal side of the arc,

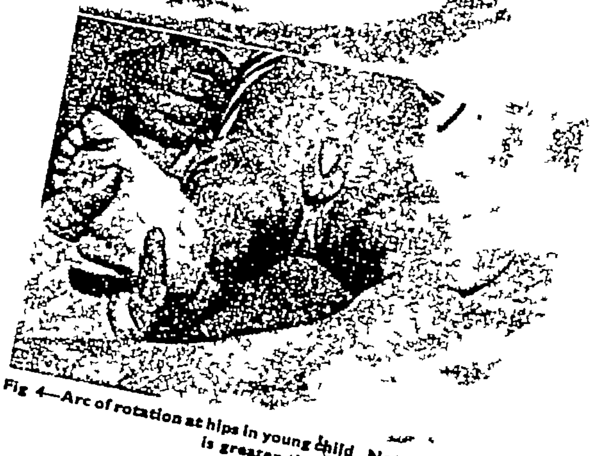


Fig 4—Arc of rotation at hips in young child Note that internal is greater than external

is that such a walks with its , internally at the hip 5)

CONCLUSION

ough most prac oners recognise there is a spon ous tendency to of these se so called rmities during I hope they find this simple useful in worried s, and that it render unneces the use of two expensive shoes—wedged and remedial cases. The simple vre of testing ion of the hips folding the legs the sleeping posi quickly reveals reason for this n cause of parental concern

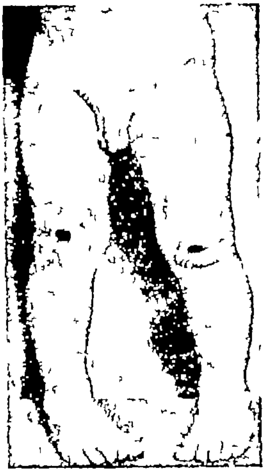


Fig. 5—Same child as in fig. 4 standing with varus feet, bowed tibiæ and inversion of hips.

wish to thank Mr K. G Moreman of the photographic of St Thomas's Hospital, for the photographs

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MYCETOMA OF THE TESTIS

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TOMA or maduromycosis is a fungus disease of distribution found most frequently in warm tries It is prevalent in many districts of India ularly round Madras) in Indonesia in South and in many parts of Africa Cases have also reported from Greece and Italy and from the States of America (Peters 1945)

on of a piece of tissue affected by this fungus destruction of anatomical structures and the nce of multiple cavities containing coloured granules, y black or yellow but sometimes red or white is generally accepted that the fungus is introduced wound, and in many cases a piece of thorn can be d in the affected tissue According to Strong (1944) ore than 70% of cases the foot is the part affected, hands, knees, and buttocks may be involved and Kirk (1940) reported a case of mycetoma he eyelid and de Almeida and Abdalla (1939) have hed 11 cases of thoracic mycetoma

Wad Medani hospital which has 300 beds and is principal *hospital in the Gezira irrigated area lying* the Blue and White Niles, 115 cases came to in the sixteen months from August, 1951, to mber, 1952. The parts of the body affected were

Part of body	*No. of cases*
Foot and leg	96
Hand	13
Elbow	1
Scalp	3
Buttock	1
Testis	1

There were 79 cases of black mycetoma, 35 of yellow, and 1 of red

A male Sudanese aged 35 was admitted to hospital on July 13 1952, with a month's history of a painless swelling of the left testicle. He had undergone an operation for hydrocele on the left side ten years previously

On examination there was a smooth enlargement of the body of the testis as large as a cricket ball There was no thickening of the cord Rectal examination revealed no abnormality and there were no abdominal tumours to be felt. The skin over the outer aspect of the scrotum was adherent to the underlying structures but there was no sinus. There was no sign of hydrocele Testicular sensation was considerably impaired. Wassermann and Kahn tests were not done.

Operation.—On July 15, 1952, the left testicle the overlying skin and the cord and vas up to the internal ring were removed in one piece

Pathology.—Section of the testicle showed that only a very small portion of normal testis remained The rest of the enlarged organ was occupied by numerous cavities stuffed with coarse black granules of mycetoma, each granule being as large as a pin's head

Recovery was uneventful

No history of trauma was obtained in this case and it is unlikely that an operation for hydrocele ten years previously had any bearing on the development of mycetoma in this unusual situation. Nevertheless it is probable that minor injury from a small thorn or similar object introduced the fungus

My thanks are due to Dr C B Drew director of medical services, Ministry of Health Sudan Government for permission to publish

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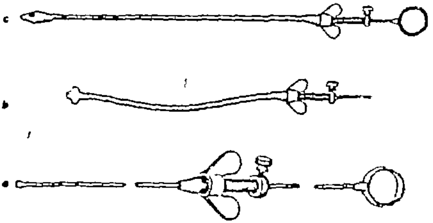
New Inventions

NEW INTRODUCER FOR THE SELF-RETAINING CATHETER

THE safe introduction of a self retaining rubber catheter of the de Pezzer or Malecot pattern depends on the fact that its expanded tip is stretched out by a metal introducer passed up its lumen. Experience has shown that the end of the metal rod sometimes perforates the tip of the catheter when the latter is being extended by it or during the introduction of the catheter Further, there is often some difficulty in keeping the catheter stretched upon the metal introducer This new instrument has been designed by Mr Joseph Atkinson, male charge nurse in the main theatre here, with a view to overcoming these difficulties.

The illustrations, drawn by our surgical artist Mr D P Hammersley show how this instrument works. It consists of two pieces (see *a* in figure) a metal rod with a small bulbous tip and a ring handle at the other end and a short length of metal tubing which forms the fixed base through which the rod slides. The catheter is fixed to the base by pushing its proximal end over a



onical cuff with a deep shoulder and by tightening a winged screw down upon the end of the catheter (see *b* in figure) Thus held securely the catheter is extended by pushing the metal rod forward to the required extent (see *c* in figure) The rod is next fixed to the base by tightening the thumbscrew down upon it

This instrument is being made in two sizes for larger and smaller catheters, and Messrs Chas Thackray & Sons of Park Street, Leeds, will produce it

Royal Victoria Infirmary,
Newcastle upon Tyne

JOHN GILMOUR
M.S Durh, F R C S
J ATKINSON
S R.N

Reviews of Books

The British Contribution to Medicine

JAIME JARAMILLO ARANGO, former rector of the National Faculty of Medicine of Bogota Edinburgh E & S Livingstone 1953 Pp 220 25s

THE author was an eminent surgeon in Colombia before he became first minister and then ambassador of that republic in London, a position he held for many years, including those of the second world war This impressive, well-illustrated book is conceived as a permanent memorial of his mission Sir Arthur MacNalty, in a foreword, tells us that it was first written in the pure Castilian prose of which the author is so complete a master It is primarily designed for the use of doctors and students in the Latin-American countries, and the English edition has been prepared concurrently

A general historical survey of British contributions to medicine is followed by a detailed study of five special subjects in which British investigators have illuminated knowledge Sir Almroth Wright's pioneer work on antityphoid inoculation, the story of the discovery of penicillin the conquest of malaria, including the synthesis of paludrine the conquest of nutritional disease, and the struggle to find a cure for cancer, including the pioneer work on stilbœstrol and other similar products with œstrogen action Dr Jaramillo Arango very properly strays at times beyond the scope of his title, and includes, out of interest an account of the history of the antibiotics other than penicillin in which few British names appear

Much of the text is written with charm and distinction, and though occasionally the story becomes complex, it cannot fail to leave a glow of national pride in the British readers, the more so because it is the appraisal of a competent foreign critic who has lived among us

Mushrooms and Toadstools

A Study of the Activities of Fungi JOHN RAMSBOTTOM London Collins 1953 Pp 306 30s

Mr Ramsbottom, D SC, who recently retired after forty years' service in the department of botany at the British Museum (Natural History), here contributes a volume to Collins's New Naturalist series, it is therefore not a textbook for use in the identification of fungi but a general account of different aspects of mycology, including history, mythology, uses, and ecology The excellent and numerous illustrations are mostly from colour photographs by Mr Paul de Laszlo, but also include nine photographs by Mr Somerville Hastings, F R C S, an aerial view of Stonehenge (to show fairy rings") by Mr O G S Crawford, and a view of the fermenting plant of Glaxo Laboratories

The chapters of greatest importance to medical readers are those dealing with poisonous and edible species, ergot, and penicillin, the last named is one of the best short accounts of this discovery hitherto published The poisonous fungus most likely to be met with in this country is undoubtedly the death cap (*Amanita phalloides*) so details are given of the identification of this species the symptoms and treatment of poisoning by it and the history of the analysis of its toxins Over a hundred years ago J Roques recommended a large quantity of either honeyed or sugared water as an antidote, and in 1936 Le Calvé[1] gave salt by mouth and by injection The former combats the hypoglycæmia and the latter the dehydration caused by the toxins An ingenious remedy—the stomachs of three rabbits and the brains of seven (both magic numbers) chopped up and administered raw in is based on the fact that rabbits are insusceptible to po by death cap eaten in small quantities and on the assu that there are two toxins, one acting on the brain and other on the liver Alleged cures might have been Dr Ramsbottom suggests, to the sugar in the jam more modern method of giving methionine to combat to the liver, and glucose to combat the hypoglycæmia not mentioned

Extrasystoles and Allied Arrhythmias

DAVID SCHERF, M.D, F.A C.P, associate profes medicine, New York Medical College, ADOLF S M D Heidelberg, M R C S, medical officer in charge of cardiographic department, Queen Mary's Hospit the East End, London London Heinemann M Books 1953 Pp 531 £5 5s

THIS Anglo-American combination of authors an exhaustive account of a subject which they have studying for many years The forms of irregular, were not properly classified until the beginning of century, before then their significance was not unde and bed was often prescribed for physiological arrhythmia Even today slow fibrillation can be m for extrasystoles and auricular flutter for sinus t cardia Less attention has been paid recently to n heart rhythms, though their diagnosis and tre are matters which confront the practitioner Professor Scherf and Dr Schott, in their opening ch on the history of their subject, show how irreg the pulse impressed the older medical writers and extensive information they thought they could from it They discuss extrasystoles first from the standpoint—considering the various sites of the known causes, their relationships with other orders of rhythm, and their many physiological, pathological associations They go on to cor explanations of the mechanism both of the extrasystole and the rarer parasystole They that the common extrasystole most probably orig in an abnormal focus activated by the normal parasystoles, they think, are produced by an aut regularly discharging focus protected by a zone of The book has some of the oddness of expression to expected of authors not writing in their native lang Though there is no actual padding in the text, th a good deal of repetition This is mainly an acc work but one that cardiologists will find useful.

Antibiotics and Children's Diseases

Seminar Organised in Paris, Sept 22–27, 1952, by International Children's Centre Chairman ALEXANDER FLEMING Paris Centre Intern l Enfance London Lange, Maxwell & Springer Pp 298 £3 3s

THIS is an account of the proceedings of a semin last September at the International Children's C Paris, under the presidency of Sir Alexander F Both clinical and laboratory aspects are discusse the section on tuberculosis is especially full Whi book contains little that has not already been p elsewhere, it is useful to have so much up to-date inf tion on the subject collected together in one volum

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Operative Gynæcology (2nd ed London 1953 Pp 902 £6)—Six years have elapsed since publication of the first edition of Prof Richard W Te book, and, as he points out, in this period not only the expected evolutionary changes in surgery taken but views have altered on such things as the uses of therapy and antibiotics, the assessment of the vaginal technique in the diagnosis of cancer, and other matt considerable importance Like its predecessor this ed informative without being verbose indeed in places almost condensed The teaching is commendably but opposite or different policies are given fair consid Professor Te Linde is so clear in his own mind about best for the patient that he is able to be dogmatic [illegible] more is given than pure operative technique he includes [illegible] necessary the fundamentals of obstetrics, and related asp of urology endocrinology, and above all pathology The bo which is profusely and beautifully illustrated, is already m valued by gynæcologists, and the new edition is welcome

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THE LANCET
LONDON SATURDAY DEC 26, 1953

Research into Pernicious Anæmia

Now that the dust raised by the discovery of folic and vitamin B_{12} is dying down it is possible to e more clearly what is known about the ætiology pernicious anæmia, and how this knowledge can be d in treatment In general outline the picture remarkably similar to what it was before, but the are different Pernicious anæmia is still a deficiency disease CASTLE[1] has put the matter very succinctly

> "the disease would not develop if the patient could effect daily the transfer of a millionth of a gram of vitamin B_{12} the distance of a small portion of a millimetre across the intestinal mucosa and into the blood stream. This he cannot do principally as a result of failure of his stomach to secrete into its lumen some essential but still unknown substance. Yet the patient may each day absorb without much difficulty the products of the digestion of many grams of carbohydrate, fat and protein from foods that in addition may contain consequential amounts of vitamin B_{12} in terms of his trivial need

The original view of the ætiology of pernicious anæmia, as expounded and developed by CASTLE in U.S.A., WILKINSON and UNGLEY in this country their many co-workers, was that for normal poiesis two factors were required an "intrinsic tor secreted by the stomach mucosa—mainly in fundus in man but in the pyloric region in hogs— an "extrinsic" factor associated with protein The intrinsic factor was thermolabile, but its with the extrinsic factor gave rise to a thermo- combination which was thought to be the actual principle, this anti-anæmic factor was stored in the liver, and passed to the bone row Patients with pernicious anæmia lacked factor because of the atrophy of the glands the fundus of the stomach so formation of the anæmic factor ceased The system as we now it still involves an intrinsic factor secreted by the ndal gastric glands and an extrinsic factor present the food It is generally agreed that the extrinsic is vitamin B_{12}, despite the surprising fact that is active when given parenterally without having acted on by the intrinsic factor KLEIN and ILKINSON[2] had originally shown that the product incubation of intrinsic factor from hog gastric sa and extrinsic factor from beef muscle was ive when given parenterally, though neither was ve alone and these and similar experiments had led us to expect extrinsic factor to have an pendent action. In retrospect these findings may e been due to the independent action of vitamin B_{12} present in the beef muscle The fact that vitamin B_{12} produces a prompt, satisfactory, and complete mission when given parenterally in microgramme doses is now established, but doses of the same order given by mouth are ineffective, very large doses are needed for a satisfactory response.[3] But CASTLE and his group[4] soon showed that vitamin B_{12} is effective when given orally in small doses if normal gastric juice is administered at the same time, this finding has been widely confirmed and concentrates from gastric juice and from other sources of intrinsic factor, such as hog stomach mucosa, have given the same effect The present hypothesis is that intrinsic factor and vitamin B_{12} interact to enable the vitamin to pass the intestinal barrier into the blood Research therefore centres on two problems the nature of the intrinsic factor, and the way in which the intrinsic factor acts on vitamin B_{12}.

Work on the intrinsic factor in the last twenty years has established that this is an enzyme separate from pepsin or rennin, and that it is a large molecule probably of protein nature prolinase,[5] aminopolypeptidase,[6] and lysozyme[7] have been suggested, but evidence to the contrary is convincing GLASS and his co-workers considered that the intrinsic factor is, or is associated with the glandular mucoprotein of the stomach, and they claim to have demonstrated the activity of such fractions in pernicious anæmia[8] and in nutritional macrocytic anæmia[9] Similarly LATNER, UNGLEY, and their co-workers[10] concentrated normal gastric juice and subjected the concentrate to electrophoresis they obtained material from two "peaks," and the more active of these—as tested clinically in combination with B_{12}—was either a mucoprotein or a mucopolysaccharide Investigations with microbiological techniques have shown that the level of vitamin B_{12} in the serum of patients with untreated pernicious anæmia is much below normal levels, thus MOLLIN and ROSS[11] found by euglena assay an average normal serum vitamin B_{12} level of 350 µµg per ml whereas patients with pernicious anæmia have levels of less than 40 µµg per ml The idea has been that the vitamin B_{12} in the food is not absorbed, and is presumably excreted, but evidence of this is not easily obtainable by microbiological methods because some vitamin B_{12} is produced in the colon by bacterial action[12] Supporting results have however been obtained by preparing a vitamin B_{12} labelled with the radioactive cobalt isotope Co^{60} HEINLE, WELCH and their co-workers[13] found that when a dose of 0·5 µg of labelled vitamin B_{12} is given to a patient who has not got pernicious anæmia, about 40% of the dose is excreted in the fæces But in 4 patients with untreated pernicious anæmia 72–90% was excreted They further found that by giving normal gastric juice or an ammonium sulphate precipitated fraction of hog stomach mucosa, excretion of a test dose of vitamin B_{12} was reduced to 29% or less. The action of intrinsic factor on vitamin B_{12} has been explained in several ways The original idea that intrinsic and extrinsic factors interacted to produce a hæmopoietic factor different from either seems to be negatived by the discovery that vitamin B_{12} is highly effective alone if given parenterally The next hypothesis was based on the discovery by TERNBERG and EAKIN[14] that normal gastric juice contains a substance that combines with the vitamin B_{12} and makes it unavailable to micro-organisms, they suggested that this "bound vitamin B_{12}" was then absorbed and that intrinsic-factor activity could be measured by estimating the "binding capacity" of the gastric juice or other material. Most work, however, supports the conclusion of PRUSOFF et al[15] that the intrinsic-factor activity of a substance is not correlated with its ability to bind vitamin B_{12}; in fact, using fractions from desiccated defatted hog stomach they found that the fraction most active in potentiating the effect of vitamin B_{12} given by mouth to patients with pernicious anæmia was the one with least vitamin-B_{12} binding capacity. Another possible mechanism might be that intrinsic factor forms a hæmopoietically more active complex with vitamin B_{12}, but CASTLE[1] considers that the evidence is against this hypothesis, too Most probably intrinsic factor specifically facilitates the absorption of vitamin B_{12} by the intestinal mucosa The results with radioactive vitamin B_{12} support this idea CASTLE and his group[16] suggest that the significant relationship is between the intrinsic factor and the intestinal mucosa, intrinsic factor is thought to catalyse some enzyme process in the superficial layer of the epithelium of the small-intestine wall which in turn is directly concerned with the absorption of vitamin B_{12} Since there is no evidence that absorption of other food substances is abnormal, this effect of intrinsic factor must be specific for vitamin B_{12} Dr FOY and Dr KONDI in their latest work on the nutritional megaloblastic anæmia of Africans, published last week,[17] had a group of patients who would respond only to vitamin B_{12} given intramuscularly, and these patients had atrophic gastritis and complete achlorhydria, whereas other patients who had this nutritional anæmia owing to vitamin B_{12} deficiency but had normal gastric secretion responded to vitamin B_{12} given by mouth, or to alteration in their intestinal flora by penicillin so that enough vitamin B_{12} was produced to give a response Thus intrinsic gastric factor seems to be necessary for the absorption of vitamin B_{12} whether taken by mouth or produced in the intestine

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The efforts of chemists have turned to producing a concentrated intrinsic factor fraction that is stable and can be applied therapeutically SPIES and his group[18] point out that such fractions, combined with a small dose of vitamin B_{12}, would provide a practical agent for the oral treatment of pernicious anæmia Active fractions from hog stomach have been prepared by PRUSOFF, WELCH, and their associates[15] in which the final protein content was only 0 03% of the original crude source, and such fractions were still not homogeneous by electrophoresis Commercial preparations of active fractions of hog stomach or hog duodenum combined with small amounts of vitamin B_{12} have now been put on the market, the methods of preparation have not been reported, but they are probably similar to those by PRUSOFF et al. GLASS and BOYD[19] have the results with one of these commercial pre in pernicious anæmia good response, with a rise of red blood-cells and hæmoglobin, was o from 60 mg. of intrinsic-factor concentrate with 15 µg. of vitamin B_{12} orally daily. It has not been shown that such mixtures will give effective tenance, and at present treatment with these preparations is very much more expensive than regular parenteral doses of vitamin B_{12} with desiccated stomach and proteolysed liver mouth used to be popular and was certainly effective, but today their comparatively high discourages their use. If these newer pr prove their worth, and their price can be reduced, treatment will again be much used But regular vision is no less necessary than with treatment BREBNER[20] has lately emphasised this his review of a group of patients with anæmia seen at a non-teaching hospital, commonest cause of major relapse was a period inadequate treatment.

The Culture and the Breakdown

IN finding expression the troubled mind makes of the material to hand Any contemporary great or trifling, can be dramatised to make anxiety dream, any current belief harnessed to hysterical manifestation Prof RALPH LINTON, in Thomas William Salmon lectures delivered last m to the New York Academy of Medicine, pointed that in fact the influence of the culture runs the manifestations of mental disorder in every The relation of the individual with his culture reciprocal he is shaped by it and he contributes its shaping As he grows up, his culture infl him in three ways—by what other people do to (especially in the way of child care and training), what they deliberately teach him, and by what he of their behaviour to other people The last is stronger influence than is often supposed, for ability of the child to compare the treatment he getting with that received by others affects valuation of himself, and helps to determine relationship with his parents We are still not sure what period the culture exercises its influence on the developing personality, though it will be during the early years of life Prof Lin notes, however, that recent research suggests infantile experiences—toilet training and patterns—are not such important personality deter minants as was formerly supposed

The influence of the individual on his culture exerted when, as an adult, he is able to accept or new ideas Since all members of a society are to much the same cultural influences, it is not ing that certain personality resemblances run thro particular societies, though of course there is general identity of personality structure all personality can be found in any society (provided it is reasonably large), but the frequency with which given type of personality appears will differ from one society to another The type of personality occurring most often in a particular society is termed basic personality ", and the basic personalities of ifferent societies naturally differ considerably. Except r cultures undergoing rapid change the basic personity will be congruous with the culture, and those who re happily equipped with it will be able to participate the culture with a minimum of frustrations and a aximum of rewards. All societies have neurotics, sychotics, and hysterics recognised by other members f the society as such, but their symptoms differ from ociety to society in ways which strongly suggest that ey have been shaped by cultural influences. Morever societies differ in the way they deal with people lowing these disorders and some make social use f particular forms of psychic abnormality. The bnormalities themselves, however, seem to crop up all societies, and as LINTON puts it "individuals ith the constitutional defects responsible for such bnormalities would be abnormal in any society." robably these defects have a physiological basis. here the personality of an individual departs idely from the basic personality of his society, tests istory taking, and analytic studies indicate that his rly experience has often been atypical for his society.

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It would be interesting, of course, to know something ore about psychoses in non-European societies, but e data are scanty. The most useful reports come om Africa, where all types of insanity found in uropeans seem to be present, though the frequencies iffer. Thus depressive reactions are exceedingly rare Africans—and so indeed, is self-reproach. The rican blames his environment rather than himself, d hence his psychotic response is more often paraid than depressive. It is noteworthy that, among lusional psychotics, literates who have had a uropean education develop symptoms essentially uropean in type whereas non-literates show the rican type of response. From this it has been argued at Europeanisation, and the resultant cultural esses is *not* a significant causal factor in psychosis. lf reproach and depressive states are rare likewise Brazilian Negroes. Among these physical catatonia ounting to waxy flexibility has been seen in patients owing only superficial social withdrawal. Satisctory cultural explanations of these differences NTON says have not yet been offered. Membership a tribe, all closely related is a great support, and y check a patient's impulse towards withdrawal ain, perhaps the violent emotional expression which se cultures permit makes self-reproach unnecessary et, though primitive peoples respect psychotics, arding them with fear and awe, there is no society, ofessor LINTON finds, where the genuine psychotic cupies a favoured social position. To exploit the vantages of abnormal behaviour one must know ry well what one is about and the inability to do is is the real test of psychosis. Medicine men d prophets who make a good thing out of their centricities do not qualify as insane.

euroses seem to be as widely distributed as psytics, though we have no clue to their relative quencies among primitive peoples. However their versality is an argument against FREUD's theory at they originate in sexual repression, for they appear in societies where expression of the sexual impulse is largely unlimited. It is more probable LINTON thinks that they result from the consistent frustration of any primary drive. In the Marquesas for instance, neurotic expressions centre round food rather than sex. In any case there is probably an underlying constitutional factor, for in all societies many people endure experiences which make others neurotic without becoming neurotic themselves.

Now evidence shows that certain types of hysteria have geographical distributions and that these often cut across racial lines. *Amok* is a form of aggressive suicide practised by males: they attack everyone they meet until they are finally killed. *latah* is a condition of complete submission, in which the patient, when startled, imitates the speech and actions of the first person he (or she) sees. *Amok* is limited to South-east Asia, but *latah* is found in Mongolia, North Africa, and the Near East, and is also a component of Arctic hysteria. Supposed spirit possession is found throughout most of the Old World, but not in Moslem countries where possession by spirits other than demons is thought to be impossible. Among American Indians *amok*, *latah*, and spirit possession are almost unknown, though conversion hysterias are common. In Europe and America the pattern of hysterical symptoms has changed in the last few generations. Spirit possession, common in the 17th century, has almost disappeared, and so has *grande hystérie*. So, too has fainting, the hallmark of the real lady; but social distinctions in hysteria are still with us: during the late war conversion hysterias were almost confined to other ranks; officers had nervous breakdowns. LINTON concludes that though a predisposition towards hysteria may be of physiological origin, its manifestations are shaped by the culture to an even higher degree than are those of neurosis and psychosis. The hysterias of course bring advantages: they are designed not only to elicit favourable response from the audience but also to inconvenience and annoy the hysteric's associates, and must be regarded either as an escape mechanism or a response to ego deprivation. It is worth bearing in mind how intolerable must be the situation, how deprived the ego, to drive the patient to such lengths.

Annotations

CHRISTMAS BERRIES

How poisonous are mistletoe berries? No doubt this question is asked in several homes and hospitals at this time of year. In one casualty department last December, a five-year-old arrived with some of the berries inside him. Hasty inquiries were made while gastric lavage was started, only to be thankfully abandoned when the pharmacist gave assurance that mistletoe was a medicinal substance. In fact mistletoe has an illustrious pharmacological history. In an 18th-century treatise it was acclaimed as "a most wonderful specifick remedy for the cure of convulsive distempers." As late as 1908 it could be described (in New York) as "a panacea in therapeutics," and it vanished from the *B.P.C.* only in the great pruning of 1949. By then it had fallen on evil days, lingering only as a vasodilator in hypertension and as a sedative—e.g., in hysteria and chorea. All the same it seems that mistletoe *can* be dangerous, but only if taken in large amounts by a small child. One death is on record; long ago a baby of 15 months was left in the care of his sister aged 6: when he was found nearly comatose, the little girl confessed that she had fed him with the berries because she found them too bitter to eat herself. After an emetic the child vomited a great quantity of berries but died soon afterwards. On

…nother occasion, a boy of 14 was found unconscious in the street, an hour after eating eight mistletoe berries It is said that the doctor suspected alcoholic intoxication, and at that season he may have had cause

Holly berries may also be sampled, but this need cause even less anxiety, for their effects are mainly purgative The only report of holly poisoning we know of appeared in our columns [1] in 1870, when a boy aged 3 ate a number of the berries He soon had bilious vomiting and copious diarrhœa, berries being seen in the motions. After welve hours he lost consciousness, but had fully ecovered next day The winter cherry or Jerusalem herry, commonly found as a decorative pot plant, another berry which may prove too attractive at iristmas-time Two species are *Solanum capsicastrum* d *S pseudocapsicum* *S capsicastrum* is the usual one l is believed to be harmless, but children have died r eating *S pseudocapsicum*, and even three or four ies can produce symptoms A 2 year-old boy died itly in Italy after eating these berries, which rently he found growing wild.[2] Vomiting was very e and was followed by convulsions and coma A winter cherry is thus the most dangerous of the three There is no specific antidote for any of these berries If any significant quantity has been taken, emesis or gastric lavage will give peace of mind. Thereafter, the treatment is symptomatic.

"SCALENE NODE" BIOPSY

It is occasionally very difficult to get histological evidence of intrathoracic disease Abnormal tissue may be sought by bronchoscopy, thoracoscopy, and thoracotomy, or by examination of sputum and pleural fluid. The search can be extended further by liver biopsy, sternal puncture, or removal of enlarged superficial ymph nodes But commonly no nodes are palpable, and the removal of the deeper, impalpable ones may seem worth while Daniels,[3] for instance, dissected out the nodes lying on the scalenus-anterior muscle in patients with sarcoidosis, bronchial carcinoma, and silicosis and found abnormal tissue in them

Shefts et al [4] have made this investigation in a very much larger series They report the results of 205 dissections in 187 patients with intrathoracic disease in whom histological evidence had not been obtained by other methods There were abnormal findings in 67 (35%) These "scalene nodes" are said to be connected with the mediastinal nodes, and it might be assumed that the pathological process in one of these two groups is always the same as that in the other But this is ıot necessarily so It is not known how commonly aseous tuberculous changes affect the deep cervical odes of patients who have no radiographic evidence of trathoracic tuberculosis, the nodes receive lymph m many sources and the tuberculous infection may ve travelled down from the throat and not up from the ıung Moreover, microscopic tuberculous changes in the mediastinal nodes are so commonly present without the patient having "tuberculosis" that, even if the infection of the cervical nodes has been by way of the mediastinum, there must still be doubt whether the intrathoracic abnormality being investigated is tuberculous Similar caution might be wise in interpreting the nodal changes associated with sarcoidosis, for noncaseating tuberculous lesions are sometimes found in the mediastinal nodes of patients with pulmonary tuberculosis

Shefts et al suggest that this investigation may be useful not only in detecting bronchial carcinoma when other methods of investigation have failed but also in detecting those proved cases of carcinoma in which the disease is too far advanced for surgical If the sole aim of resecting bronchial carcin to eradicate all cancer tissue, this prelimina might save some useless operations But remo affected lobe or lung in patients with small metastases may, even if it does not postpone make what is left of life happier. Additional from the pathologist, although refining the diagnos not help either in treating the patient or in the course of his illness. Excision of deep cervic nodes may be safe and cause the patient only discomfort, but this investigation should perhaps reserved chiefly for obscure intrathoracic where histological evidence is necessary for treatment

PREPARATION FOR TONSILLECTOMY

" . the emotional equipment required for adequately with a hospital experience is no differe that needed in dealing with all the other problems

TRUE enough, but the research team at the College, New York, who make this observation aware that life, taking us by surprise, can rattle our emotional equipment considerably may respond to such an experience with neurosis or psychosis, but the child usually responds with beha disorders

It is no new finding that admission to hospital tonsillectomy can be a harmful experience for and the research team, under the direction of Dr. Otto Faust, tried to find out whether careful preparation handling reduces the emotional injury. For one or another their original plan for a controlled had to be given up, but in the collected papers form the basis of their final report,[1] to which Mac Keith refers in a letter this week, they set methods they used to reassure children and to r them to their former pursuits free from symptoms. Briefly, their method was to choose laryngologists and anæsthetists with experience of sympathy for, children, they ensured that the atmosphere was kindly, they allowed one paren remain in hospital with the child throughout his and they sent a social worker to visit the child in home before operation, to tell him what to expect

There were 140 children aged 3–8 in the and the key people in preparing them to face o confidently proved to be the social worker and anæsthetist The social worker visited the home less than a week before the child was due to be made friends with him and his mother, and noted setting in the family She described to the child size of the hospital, what he would see as he entered doors, the ride in the lift, the way the doctors nurses would be dressed (which some children frightening), the ward, the other children, and the of bed he would sleep in (for some, having from a cot to a bed, are affronted by the cots in a ward) She also advised him to take a favourite toy him Thus interview fortified him for his arrival hospital, especially since his mother usually went him

On the evening before his operation the a woman—visited him and took pains to gain his dence She found out whether he had had an before, and judged for herself how he felt about it; also learned, from conversation with the mother, he had been prepared for the operation at home—w in fact, the suggestions he had received had been or accidental positive or negative She explained him carefully that he would go to s except for a sore throat afterwa and she let

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[1] Reducing Emotional Trauma in Hospitalized Children. the departments of pediatrics and anesthesiology. Medical College Albany, New York. 1952 Pr

the mask, telling him that he could hold it over his himself, and that breathing the medicine on it would him fall asleep She described simply the queer dizzy feeling he might have while falling asleep, and told him about the theatre and the sort of clothes *the doctors would be dressed up in*

day she came herself to take him to the operating e, and faithfully kept her promise to let him hold mask. She seldom found that a child wished to lift mask or throw it off and if a child became nervous a reassurance, and the placing of her own hand over not as a restraint but to give confidence—usually to calm him Premedication was slight, or not at all She found that with this method the tion time was shortened, the stage of excitement was severe (usually lasting only a second or two) and child needed less of the anæsthetic agent She also d that such an experience far from diminishing a d's courage, usually reinforced it Having taken the it gamely he rose in his own esteem

Some other general principles were put into action with e children It was found that rectal temperature ng was alarming and so of course were enemata *were given up, and the temperature after the* tion was taken only at night in the groin or the a. Since the children dreaded injections, these too o avoided, except for an injection of atropine just re operation and a needle prick for hæmoglobin imation

The social worker visited the child at his home ten days the operation and again two or three months later, see whether he was showing any evidence of increased y She estimated that, of the 140, 13 showed favourable behaviour changes but some of these, use they had belonged to a group originally intended controls, had not been so carefully prepared for the etic as the rest of the experimental group The ren treated with consideration for emotional factors less evidence of trauma than those who were not than half of the 140 showed behaviour that was r unchanged or improved, and about a third showed mixed response being improved in some traits and rbed in others in most of these cases, however the r thought that on the whole the child was better d. The younger children in the series showed more milder adverse behaviour traits than their seniors.

BRONCHOGRAPHY IN PULMONARY TUBERCULOSIS

IT is a commonplace that pyogenic inflammation in lung may be followed by bronchiectasis, but the uency with which this takes place in tuberculosis often underestimated. Apart from the dilatation an episode of bronchial occlusion during the ry infection, bronchiectasis is often produced the resolution and repair of the long-drawn out onia of pulmonary tuberculosis. There is usually point in attempting to distinguish between the shadows the active pneumonia and those of the fibrous repair may follow, but it is a fact that bronchiectatic areas lung may produce an appearance deceptively similar active tuberculosis, particularly in upper lobes which ve been subjected to collapse therapy and that dowing thought to represent infiltration may largely from bronchiectasis.

The frequency of these events cannot be appreciated less bronchography is widely practised on the tuberculous and there are good reasons for not doing this The most valid practical objections are the difficulty the retained Lipiodol may cause in future interpretation of the chest films, the danger that its presence may mask a spread of the disease, and the possibility—even though remote—of the investigation provoking a flare up of the illness On the other hand, should the surgeon wish to know the state of the bronchi before operation it may be necessary to undertake bronchography in spite of these risks, and a new medium for bronchography has recently been introduced which is particularly suitable *for these cases Dionosil is a suspension of diodone in* oil or water and it is absorbed from the lung within a few days. It thus overcomes one of the main disadvantages of lipiodol, and there have been favourable reports on its use[1,2] At the moment, however these media have certain disadvantages not encountered with lipiodol. They are more irritating to the bronchi and anæsthesia has to be more cautious and complete, and therefore more time-consuming Febrile reactions often follow within twenty four hours accompanied sometimes by bronchitis pneumonia or collapse of the lung these complications may not be serious, but they are certainly unwelcome and may tend to restrict the use of these media to patients in hospital As they are less viscous than lipiodol the new media can be introduced through a smaller needle or catheter and yet they do not run as readily into the alveoli They are not quite so radio-opaque as lipiodol but the contrast they provide is usually adequate. They are still being developed, and if they can be made less irritating and more opaque, they may prove a valuable aid to the planning of treatment and the evaluation of its results.

SCIENCE TEACHING AT SCHOOLS

THE shortage of teachers of mathematics and science in the schools which has caused concern since the end of the war is likely to get worse in the next few years when the post war bulge in the birth rate will affect the secondary-school population.[3] A report by the National Advisory Council on the Training and Supply of Teachers[4] describes the findings of a subcommittee which worked under the chairmanship of Sir Charles Morris It ends by saying:

> We consider that the shortage of graduate teachers of mathematics and science constitutes a national problem we feel bound to emphasise our conviction that unless enough men and women with suitable abilities and *qualifications come forward to teach in schools there must* be serious long term effects both on the general quality of education of the nation and on the future supply of scientists and technologists.[4]

The report gives an estimate of the average annual requirements of graduate teachers of mathematics and science in grant-aided schools in the period 1950–60 This is 580 a year for the five years 1950–55 and 1020 a year for 1955–60 These figures are on the low side for the subcommittee takes as its standard the staffing conditions prevailing in 1950 though like other authorities, it does not regard these conditions as satisfactory The deficiency in teachers is not only quantitative but also to some extent qualitative: in 1953 only 18 men with first-class honours in mathematics or science left university departments of education compared with 48 in 1938 and the first-class and second-class honours graduates together formed only 30% of the total in 1953 compared with 60% in 1938

The council *suggests increasing the attractiveness of* school teaching by improving its prospects and working conditions—for instance, by providing laboratory assistants. At present the schools are at a disadvantage in competing with the universities and industry for the most promising graduates. Unless however the total number of graduates can be increased this policy would involve robbing Peter to pay Paul and Peter himself

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1 Don, C. J *Brit. J Radiol.* 1953 26 573.
2. McKechnie, J K *Tubercle*, 1953 34 271
3. Schools under Pressure. *Planning* 1953 19, 208
4 Graduate Teachers of Mathematics and Scien the National Advisory Council on the of Teachers. H.M. Stationery Office

is not well placed. The fact is that there is an all-round shortage of good science graduates, and some university teachers doubt whether suitable students can be recruited in larger numbers than at present For this there seems o be no quick and easy solution

Where a boy or girl has early made the decision to come a doctor, inadequate teaching of science at school is unlikely to deter him or her from trying somehow to pass the first M.B examination before going to a university or medical school. But lack of suitable teachers at school may prove a serious handicap to the boy who decides late. At present, unfortunately, those who have passed the first M.B examination have a better chance of gaining admission to a university or medical school than those who have not; and if this policy is to be maintained the universities will at least have to make sure that failure in this examination due o inept teaching does not unfairly debar a candidate om admission The alternative would be to restore to universities the responsibility for teaching the first M.B subjects to all students This would have the effect of prolonging more general education at school, and would put all candidates on a more equal footing, but it would also extend the very lengthy professional training, and transfer to the universities some of the staffing difficulties which now beset the schools University and school authorities will do well to examine this problem together before the increasing dearth of teachers makes action inevitable

HEPARIN AND ATHEROMA

THE use of heparin in the treatment of coronary disease and the development of synthetic analogues, such as dextran sulphate,[1] raise an interesting question The rationale of using heparin to combat coronary thrombosis was that it prevents clotting Biochemists, on the other hand, have been quick to suggest another type of action on atherosclerosis, due to the very far reaching effects of heparin injection on the circulating lipoids—an action which is not shared by dicoumarol and phenylindanedione

In 1943 Hahn [2] observed that the turbidity of alimentary lipæmia in the dog was almost immediately cleared y an injection of heparin, but adding heparin solution drawn blood had no effect on the turbidity Seven years later Anderson [3] found that the plasma of a heparin-injected animal would clear lipæmic plasma in vitro The mechanism of this action is complicated It has been shown to be due to the coupling of a plasma constituent with heparin by an enzyme present (in the rat) chiefly in heart and lung tissue The resulting "clearing factor," in the presence of yet another plasma constituent, can reduce the turbidity of lipæmia [4]

The detergent-like action of heparin clearing factor (H.C F) might have remained a curiosity if it had not also been observed [5] that heparin injection brings about redistribution of the lipoprotein fractions determinable with the ultracentrifuge, and that in this process there is a pronounced reduction of that group of low density lipoproteins which the Donner Laboratory workers have regarded as closely and perhaps causally, related to atherosclerosis [6] The statistical evidence for this view has been severely treated [7], but the fact remains that a concentrate of this fraction, prepared by cholesterol eeding in the highly atheroma susceptible rabbit, can aduce cholesterol atheroma when injected into other animals,[8] and that administration of heparin substantially protects rabbits against cholesterol feeding.

Speculation has followed these findings. It possible that differences in the activity of the system at some point in the chain might account specific differences in susceptibility to dietary (since the rat is both highly resistant and a good pr of H C F, while the rabbit is highly susceptible and poor producer [4]) and even for individual and age ences in human susceptibility.[10 11] These are interesting but premature The comparative of the response to heparin in different laboratory is now being elucidated. It shows signs of inconveniently complex as such relationships usually

Injection of heparin has no effect on the turbidity rabbit plasma,[4] but in some strains at least it lipoprotein distribution [5] and protects against It has also been found that, despite the failure of he to clear rabbit plasma, it brings about a striking selective increase in the electrophoretic mobility of lipoprotein fractions, especially the β component is the fraction affected chiefly by cholesterol fe This enhancement of mobility disappears be critical blood-lipoid value—either because an constituent also disappears below that value or more probably, as a result of a change in the concentrations of different lipoids. Rabbit plasma heparin injection both clears lipæmic dog or plasma and accelerates its β lipoprotein.[12] The scence of lipæmic rabbit plasma clearly differs in important respect from that of dog, or normal lipæmia, since it is not cleared even when mixed nine times its volume of active H C F-containing pig plasma Rat plasma is sometimes active as a clearing agent [4], but this is occa- observed even in rabbits [14]. There are signs that plasma can occasionally couple heparin added to vitro, and therefore presumably may contain "tissue factor," the enzyme responsible for the process [4 14 15] Block et al [16] found that clearing more slowly after heparin injection in ather than in normal people

From this confusion the only clear inference be that if heparin does protect against atheroma mechanism by which it does so is more closely the ultracentrifugal and electrophoretic changes which produces than to the dissolving of chylomicrons leads to optical clearing Physicians will probably to wait until the biochemists have finished. But apart from the great importance of differences in animal and human susceptibility to from a high cholesterol diet, to which the study heparin may contribute much, the use of heparin treating or preventing coronary disease may, on basis of such work, prove to be twofold. The and even more the lipoprotein-accelerating, actions heparin in the normal person occur with ver lower doses (10–20 units per kg body-weight) than anticoagulant action It would be interesting to kn supposing that heparin really reduces the incidence coronary attacks, how far low doses of this order (they would need to be very frequent), and how action of heparin compares with that of which have no such physicochemical effects on metabolism

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Special Articles

THE NURSING OF ADOLESCENTS IN ADULT WARDS

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o some extent all patients in a ward are living in ormal circumstances. But adolescent patients have cope with the double abnormality of illness and lescence From time to time parents and teachers e expressed doubt as to the wisdom of putting lescents in the same hospital wards as adults

n adolescence the imaginative faculty is heightened l to some extent distorted, and introspection tends play a large part in conscious thought. Is there not, refore a risk that adolescents in a ward, who inevitably m a small proportion of its population will be essively spoilt by their elders, or will feel lonely earing in mind the fact that loneliness is not neces lly overcome by association with people but with ple of the same age or outlook?

nother ground for disquiet is the conversation and eriences to which the adolescent patient may be osed Particularly in surgical wards sights and unds, which are inevitable, cannot always be kept m the young Fear of the unknown and of what sees but has not experienced is always powerful, re especially in adolescence It is no part of a pital's duty nor that of the hard pressed nurses to sor conversation between patients On the other nd, detailed discussion of symptoms and forms of atment often make terrifying hearing to the young part entirely from the possibly unedifying advice en by some adults on matters of sex This is not to ply that the conversation of adolescents among mselves cannot and does not reach at times a pretty r level but it is far easier to argue against one's temporaries—who can be regarded as being as orant as oneself—than to reject the dicta of the ult who may claim to have experience and whose ars, however unjustifiably appear to lend authority his remarks.

To discover whether these doubts are in fact well unded I sought the opinion of matrons and sisters on ese points. It has not always been possible to extract m the replies to our questionnaire information which n be exactly classified, as the use to which wards are t changes from time to time and the figures quoted e accurate generalisations rather than precise statistics e views expressed were sometimes an agreed view t forward by the matron on behalf of her ward sisters d sometimes the views of the ward sisters themselves.

NUMBER OF ADOLESCENT PATIENTS

The inquiry covered 3954 beds contained in 105 wards. 0 of the beds were occupied by adolescents between e ages of 12 and 17 (9·08%) I have omitted figures r long stay patients and for wards likely to consist in e main of adolescents—for instance ear nose, and roat. The information provided therefore is based on neral medical and surgical wards. The beds were vided as follows

Ward	No. of beds in ward	Adolescents No.	Adolescents %
emale medical	881	60	6·8
surgical	1200	107	8·9
ale medical	805	97	12·05
surgical	1068	95	8·9

he hospitals from which these figures were obtained are pread over the whole of England and Wales and there oes not appear to be any variation according to district.

Of the 160 replies received 137 considered that adolescents and adults should be nursed separately, 13 preferred to nurse both together Where the replies took the form of a single letter expressing the view of a number of ward sisters it has been treated as a single reply and in every such case preference was expressed for separate nursing

NURSING OPINION

The following general points emerged from the inquiry

All agreed that the adolescent girl ought never to be nursed in a gynæcological ward, and it was generally felt that the risk of fear and of less pleasant forms of conversation was greater in female wards than in male because women were less careful and considerate of the younger members of the ward than men.

Many replies expressed the view that the adolescent (particularly in the male ward) became spoilt if his stay was more than a few days.

Difficulty is experienced in some wards where adolescents during their convalescence irritated the older patients by noise, playing games and so on

A strong preference was expressed by a large majority for the provision of an adolescent annexe or ward and it was clear that most ward sisters took considerable care to segregate the younger patients, either by curtains or by the use of verandas or by keeping adolescent patients in beds next each other

In hospitals for long-stay patients such as sanatoria and orthopædic hospitals, the situation is different for educational and other provision is made for young patients which is not possible in a general hospital But the replies to my questions make it clear that the percentage of adolescents in general hospital wards is substantial, and this fact coupled with the overwhelming weight of opinion in favour of segregation expressed by those most directly connected with the life of the ward, suggests that a problem exists of sufficient size to justify fuller and more detailed consideration than has been given it hitherto

MEDICAL RESEARCH IN THE COLONIES

PUBLIC attention is drawn to the British Colonies chiefly by things which have gone wrong in most of these territories affairs are going rightly and therefore remain unnoticed Development of a more prosperous and advanced way of life is being assisted by substantial payments from the British taxpayer through the Colonial Development and Welfare funds. Part of these funds is devoted to medical research, and the ways in which this is applied are shown in the latest report of the Colonial Medical Research Committee.[1]

MALARIA

The disease which has received most attention is malaria which has been studied in Borneo Malaya, East Africa West Africa Trinidad and the West Indies —in fact all round the world except in the Pacific islands which fortunately are free from it. Some of the work is directed primarily against the mosquitoes which transmit the malaria parasites, this includes careful studies of the habits and breeding places of the various species of anopheles, of methods of making the breeding places unsuitable by partial clearing (as with *A leucosphyrus* in Borneo) and of the practicability of destroying the adults with gammabenzene hexachloride ('Gammexane') and D D T (as in Trinidad Malaya and elsewhere) An investigation carried out at Ilaro in Nigeria during the last five years shows that it is quite feasible by residual spraying of gammexane to reduce malaria to negligible proportions with considerable falls in the crude and infant death r
but the average cost of 4s 9d. per head per year
low by Western standards, is too high f

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[1] Colonial Research, 1952–53. Colonial mittee Eighth Annual Report. C Office. Pp 268 1s 6d

to be generally applicable in the poor countries of Africa

Other work is directed chiefly towards the malaria parasites as they occur in man. Therapeutic trials of new antimalarial drugs have been carried out in Nigeria and Malaya, the chief tests have been on pyrimethamine ('Daraprim') and the 4-aminoquinolines such as chloroquine and amodiaquin In endemic areas (e g, tropical Africa) the chief sufferers are always the children, who have repeated attacks and many of whom die either from malaria or from other causes It has always been debated whether those who survive and reach adult life continue to be harmed by persistent low-grade infection or whether they have become so completely immune that it is not worth while, or even desirable, to protect them from further infection by controlling or eradicating the parasites Decisive evidence may be obtained from a scheme for an isolated district of East Africa where malaria will be wiped out by insecticides and chemotherapy, and the effect on the health of the indigenous population will be carefully studied.

VIRUS DISEASES

Considerable funds and effort have been given to virus research, especially to the control of *yellow fever* Two large institutes, at Entebbe in Uganda and near Lagos in Nigeria, are devoted to this purpose Thanks to the efficient vaccine which was developed during the 1930s by the Rockefeller Foundation it is now possible to protect individuals and whole communities, but there are still many interesting problems concerning the maintenance and dissemination of the virus by mosquitoes and monkeys in forest areas, from which it may later spread to man

Studies on *poliomyelitis* have been made in Uganda, the infection is probably widespread among Africans, but it seldom causes ill effects in them

Scrub typhus and similar infections have been studied in Malaya in collaboration with a U S army medical research unit, owing to interruptions caused by banditry, part of the work was done in Borneo

Relapsing fever and its dissemination by ticks has been studied in East Africa This infection is so common in many areas that the Africans in those parts become immune from repeated minor attacks, but newcomers to these districts—e g, immigrant labourers—have repeated severe bouts of fever which are always deleterious and sometimes fatal In the first world war it caused many deaths, and it is still a menace In this case, as in other insect borne diseases such as malaria and sleeping sickness, much help in tracing the particular species responsible for transmission has been received from a new organisation for identifying the blood found in the insects' stomachs This is dried on filter-paper and sent to a central laboratory at the Lister Institute There a great collection of sera from animals of all kinds has been accumulated during the last few years, and appropriate antisera have been prepared By special precipitin and other tests it has been possible during the past year to identify the source of over 5000 blood samples sent from Trinidad, Kenya, Tanganyika, Nigeria, and other parts of the world

FILARIAL DISEASES

Loiasis, the filarial infection which is the cause of much annoyance to Europeans and Africans in the forest areas of West Africa, has been studied at Kumba in British Cameroons The breeding places of the mangrove fly, chrysops, which transmits the infection have now been identified, and valuable information is being obtained about the habits of this pest, which will [illegible] it to be controlled and even eradicated [illegible] spread filarial infection due to [illegible] which causes *elephantiasis* of [illegible] has also been studied in Tanganyika, [illegible] Malaya Diethylcarbamazine administered by mouth

to all the members of an infected community probably reduce the infection to negligible at which level it might be unable to and so might become extinct Unfortunately often causes nausea and other minor toxic effects make the treatment unpopular and community The cost of treatment would also deterrent to its widespread application

LEPROSY

Leprosy is widespread in Africa and in Malaya research-workers to study it are difficult to because of the slowness in obtaining results intractable chronic condition and because of the tion which such work often entails. Most investigations have been carried out, Uzuakoli in Nigeria, where it has been shown oral administration of diaminodiphenylsulphone effective, simple, safe, and widely practicable treatment Thiosemicarbazones, such as (T.B 1), may be useful in special cases, esp patients who have become allergic to sulphones, they require close medical supervision during the weeks Isoniazid, which produces such dramatic in tuberculosis, has proved of little value in

OTHER DISORDERS

Besides the infections with which unfo tropics teem, other causes of ill health have been studied. The condition among African children is often called *kwashiorkor*, and which is by œdema, dermatitis, anæmia, and s hair, can be successfully treated with a high diet, but the provision of such a diet is often since in many parts of Africa milk is not o any large quantity Work at Kamapala in U has shown that even young children will diets of soya bean and other plant protein W this and other nutritional problems is being und at Fajara in Gambia, where a research station has established by the Medical Research Council

Attention has also been given to the problems of hot climates, especially by the Hot C Physiology Research Unit at Oshodi in Nigeria carefully designed investigation has exploded the fallacy that frequent drinking is bad, on account of general physiology and of water economy it is be to take frequent small drinks than a few large c the same total volume

Medicine and the Law

Forceps Left in Abdomen

A 64-YEAR-OLD woman who underwent an operation in a Birmingham hospital last month days later, and at an inquest[1] on Dec 10 her dea said to have been accelerated by a pair of artery that were left in the abdomen at the operatio gynæcologist said in evidence that he was not tol a pair of forceps was missing after the operation 36 hours the patient's condition was satisfactory deteriorated later, though her symptoms were unusual after such an operation The theatre sister that the swabs were checked and found correct, but was told that a pair of forceps was missing She that they were still attached to the cyst that had removed and she had intended to check this but to do so The coroner commended the hospital ties and the theatre sister for their frankness coroner's officer who had dealt with the matter verdict of accidental death was recorded added a rider recommending an person should be responsible for a c on all and swabs at all future operations."

[1] Manchester Guardian, 11, 1953

Before Our Time

LIFE OF THE SHAWL

DOUGLAS HUBBLE
M.D Lond M.R C P
DERBYSHIRE ROYAL INFIRMARY

is medical mythology of the 16th and e seat of melancholy lay in the liver, and the spleen Depression was con hypochondria, and the frequency with disturbance accompanied melancholy ttle should be bold enough to question en taken as a sufficient proof of a ypothesis.

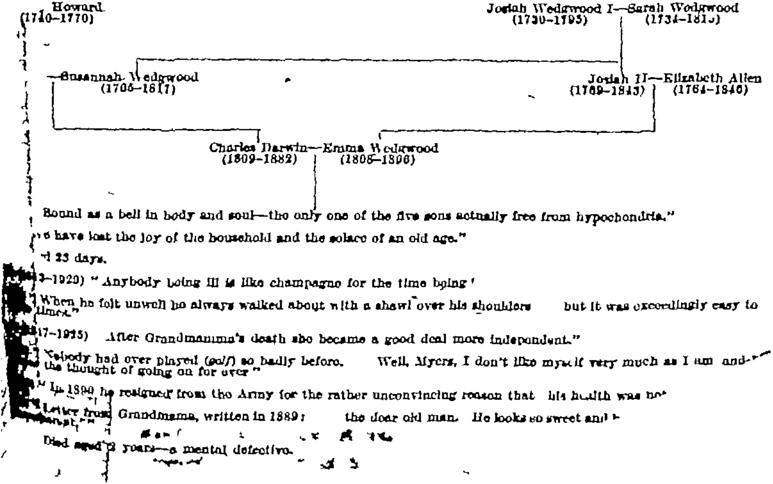
tury hypochondria was as fashionable ty today and in 1790 Erasmus Darwin, Charles, wrote: the hypochondriac indigestion and consequent flatulency ant of pleasurable sensation' These o be accepted until the 19th century Charles Darwin suffered from hypo had its popularity waned, but the on a more sinister meaning In 1873 is *Principles and Practice of Medicine,* the name hypochondriasis has very as indicating the character of and seat while the *Oxford English Dictionary* tually defined it 'as chiefly charac tient's unfounded belief that he is some serious bodily disease This d can now be elaborated by observing preoccupation with his bodily function some environmental overcare which ates his own apprehension, that it is notion that the hazards of ill health by the exercise of precaution and that perpetuated by some immaturity in the patient

ming testimony in Charles Darwin's s children's reminiscences, and in the n of family letters that his illness was ical Much of the evidence was collected in my article in this journal in 1943 where it was shown that his illness provided the exact conditions which were essential to his achievement his disordered and sleepless nights allowed his laborious mind to brood in solitude over a generalisation, while two hours *observing and recording in the morning* would expose the night's hypothesis to realistic examination and complete the day's work It was assumed too that the immaturity of Darwin's personality provided sufficient explanation of his hypochondriasis.

There was then no published evidence as to the existence of any environmental overcare which equalled and enhanced his own apprehension. This deficiency has now been made good by Mrs. Raverat's delightful book *Period Piece* This book completes a family record which spans the 19th century, and without it the tale was but half told The modern descendants of these great Victorians may protest their distaste for such chronicles (Mrs Raverat tells of an anti Darwin league formed by those who have 'inadvertently married Darwins'; Emma Darwin might suitably have been chosen as the first president, for she wrote in 1879 irritated by a long discussion of the 200 year Darwin pedigree, I don't know how it is, I should care *a little* if it related to Wedgwoods) Yet they are social documents of great value The fortune built by Robert Darwin in his Shrewsbury practice was sufficient to maintain his children in comfort his grandchildren too shared the economic security then enjoyed by the English upper middle classes. But the grandchildren were not typical of their class or time They had little enthusiasm, individuals excepted for art or for religion and in their preoccupation with natural phenomena they were apostles of science and disciples of the spirit of inquiry, true forerunners of the 20th century

The first family tree (see below) shows Charles Darwin's family and its ancestry through three generations. Ten children were born to Emma and Charles Darwin, and of these, seven reached adult life. Of the five sons George, Francis, and Horace had careers of great distinction and were knighted for their varied scientific achievements. A fourth son Leonard Darwin, is still well *remembered as the president of the Eugenics Society* and of the Royal Geographical Society Such facts as these

FIG I—DARWIN FAMILY TREE


Howard
(1710–1770)
Josiah Wedgwood I—Sarah Wedgwood
(1730–1795)
(1734–1815)
—Susannah Wedgwood
(1765–1817)
Josiah II—Elizabeth Allen
(1769–1843)
(1764–1846)
Charles Darwin—Emma Wedgwood
(1809–1882)
(1808–1896)
Sound as a bell in body and soul—the only one of the five sons actually free from hypochondria."
e have lost the joy of the household and the solace of an old age."
d 23 days.
-1920) "Anybody being ill is like champagne for the time being'
When he felt unwell he always walked about with a shawl over his shoulders but it was exceedingly easy to illness."
17-1935) After Grandmamma's death she became a good deal more independent."
Nobody had ever played (golf) so badly before. Well, Myers, I don't like myself very much as I am and the thought of going on for ever"
" In 1890 he resigned from the Army for the rather unconvincing reason that his health was not
Letter from Grandmama, written in 1889: the dear old man. He looks so sweet and
Died aged 2 years—a mental defective.

seemed to justify the conclusion that in the happy family life at Down House the Darwin children grew to serene and undisturbed fulfilment It appeared that even the continued illness of Charles brought his children nothing but gain: it gave them more of his delightful company, it ensured regular living and an ordered existence, and it required of each of them those small daily sacrifices which are the necessary accompaniment of a happy communal life. The new facts supplied by Mrs. Raverat not only allow a further assessment of the factors contributing to Darwin's hypochondria, but demand consideration of the astonishing ill health displayed by his children

Charles's Health

The only hypochondriacal illness suffered by Charles before his marriage was at Plymouth in 1831, when for two months he waited in wretchedness for the *Beagle* to set sail.

"These two months at Plymouth were the most miserable which I have ever spent, though I exerted myself in various ways. I was out of spirits at the thought of leaving all my family and friends for so long a time, and the weather seemed to me inexpressibly gloomy I was also troubled with palpitations about the heart, and like many a young ignorant man, especially one with a smattering of medical knowledge, was convinced that I had heart-disease I did not consult any doctor as I fully expected to hear the verdict that I was not fit for the voyage, and I was resolved to go at all hazards"

Charles was a good observer and in these few sentences he recognised the antecedent emotion, the disturbing physical symptom, and the peculiar suggestibility of the one-time medical student and the doctor's son He shows his courage, too, which he was to prove many times in the [illegible] dangerous years which followed

He remained well until after his marriage in 1839 He became ill in the following year during his wife's first pregnancy and was incapable of sustained work throughout the succeeding two years From the published correspondence it can be concluded that, thus early in their married lives, the life long rôles of husband and wife were already determined. He was the invalid incapable of social activity, and she was the devoted nurse who in Maria Edgeworth's words "was debarred from all London gaieties and all gaiety but that of her own mind by close attendance on a sick husband" London then was without attraction for both, and, since Robert, his father, had little hope that Charles would regain his strength for years to come, they moved in 1842 to their country refuge at Downe Nursing was Emma Darwin's métier "She was a perfect nurse in illness Her self-command never gave way, and she was like a rock to lean on, always devoted and unwearied in devising expedients to give relief, and neat handed and clever in carrying them out" Mrs Raverat is both more explicit and more percipient 'I have sometimes thought that she must have been rather too sorry for her family when they were unwell A little neglect or astringency might have done some of them a world of good" In the Wedgwood enjoyment of sickness lay the emollient influence which fixed irreversibly Charles Darwin's hypochondriacal habit The perfect nurse had married the perfect patient

It is not surprising that many of his friends, accepting his appearance of robust health as better evidence than his recital of agonising nights and valetudinarian days, diagnosed his disorder as hypochondriasis Charles mildly protested in a letter to Dr Joseph Hooker (June 13, [illegible]) "Everyone tells me that I look quite blooming [illegible]tiful, and most think I am shamming, but you [illegible] an one of these" Such mild acceptance of [illegible] without an outward aggressive reaction [illegible] Charles Darwin He ha[illegible] [illegible]thoritarian

father, to discharge a
much-travelled autonomic
his gastro-intestinal

If an aggressive reply to
prints appeared to be deman
Butler attacked his good fai
in a rare moment of anger he
of his children, then he wo
agony of mind and intestine
accepted advice that a rep
the other, craved fo
son He could, however, be
lished statements, as if unaware of
would be aroused, and when the
there was always the redoubtable
sharpened "teeth and claws," to
his theories

The Sign of the

The family life at Down House
observers, and by participants, has
hundred years as an ideal
was economic security to a
modern eye envious
man's plenty and
psychologists of
needs of growing children
assured all are
no m
House
of a good thing Affection in excess
security itself breeds a fear of

Of the seven Darwin child
only two escaped hypochon

Annie, the eldest daughter,
10, and four years later He
taken ill with an undiagnosed
year, convalescent for a further
for the rest of her life
recommended breakfast in bed,
there till she died at the age of 86.
queen of invalidism, ill health
solitary subject was her patien
Litchfield Richard's health was
obviously wiser for him to
sovereign enveloped him in a
windows were opened, and req
food while more foolish men drank

Emma supplied one enviro
hypochondria with her Wed
her calm practicality, and her
she was no doting mother, being
mentality nor to exuberant
Charles contributed the other
morbid wish to love and to be
Darwin, wrote, "he kept up
manner towards us all his life I
he could do so with such an
are, but I hope he knew how
loving words and manner" And
describing his behaviour dur
could hardly bear to have him in
of tender sympathy and
agitating" By this time Charles's
for his children had been
Annie. She died at Malvern
for a water-cure in the care of
worsened Charles travelled to
who was expecting to be
Charles was heartbroken when
five years later, writing
weep for her

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